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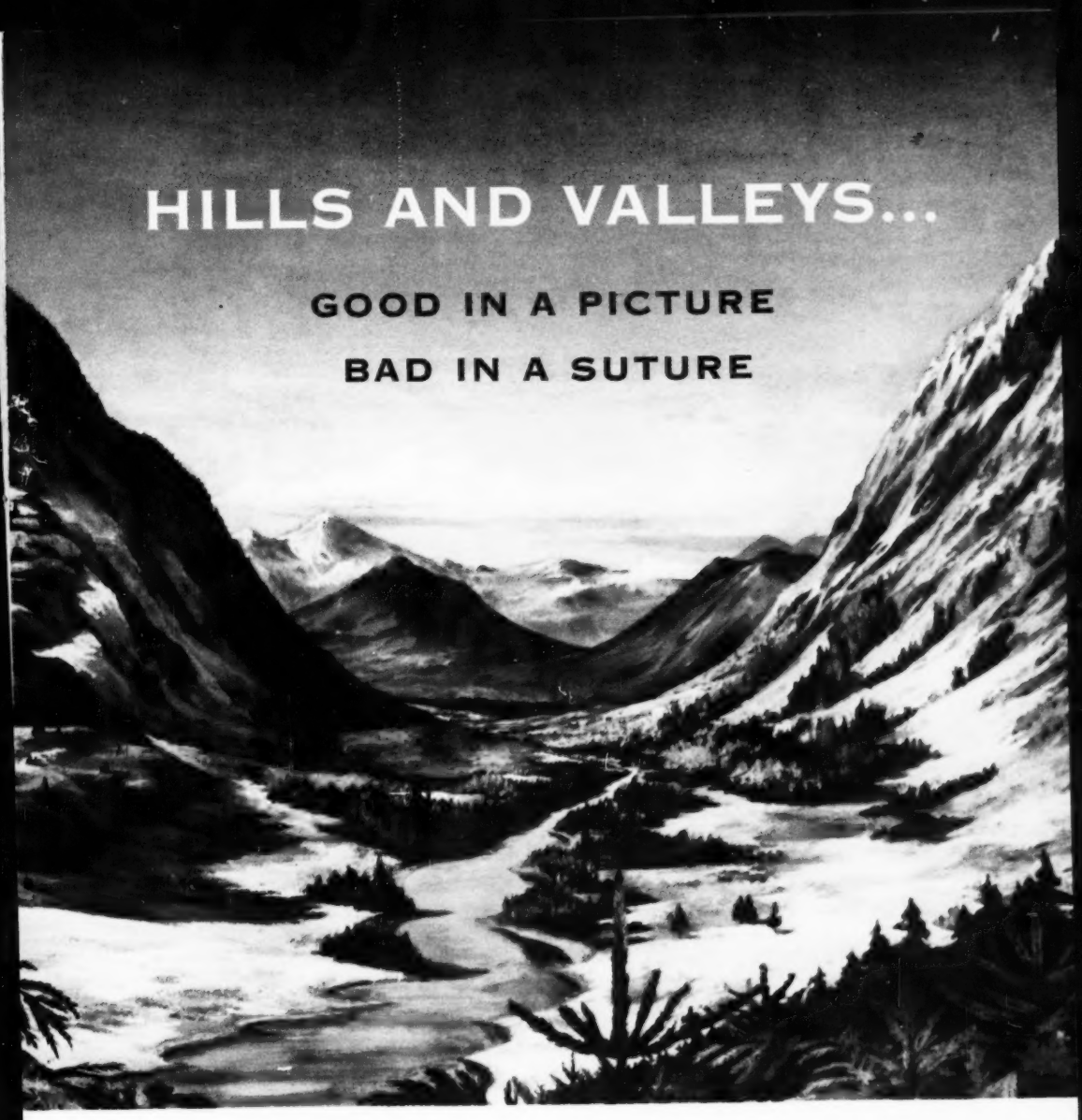

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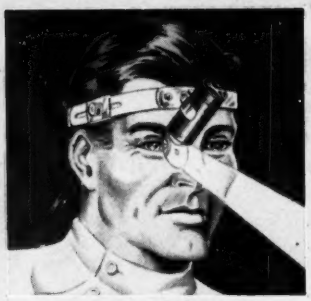

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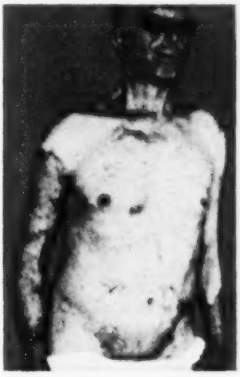

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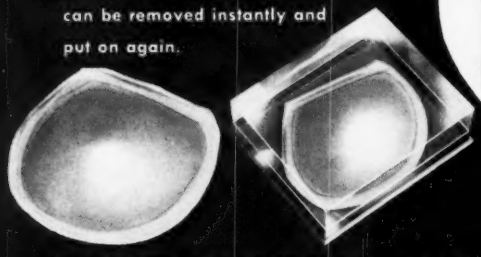

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VOLUME 67 SEPTEMBER 1953 NUMBER 3

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CRITIQUE OF ARTICULAR REPLACEMENT

S. S. HUDACK, M.D.
W. H. McGAW, M.D.
W. S. DUNCAN, M.D.
J. E. BROWN, M.D.
S. G. STUBBINS, M.D.
AND
F. R. HOLZWORTH, M.D.
CLEVELAND

INVESTIGATIONS on articular replacement were undertaken as a result of discussions with the late Clay Ray Murray. He had for a long time been unhappy about the clinical outcome in subcapital fractures of the femur. Through long-term follow-up at Presbyterian Hospital it became clear that pinning, either open or lateral, was not the answer. The same was true with grafts across the fracture site or multiple drillings. Muscle transplantation, to give increased vascular supply, to the femoral head was likewise ineffective in altering the long-term clinical course.[1] In high subcapital fractures with adequate reposition, pinning, and, sometimes, osteotomy, the results were poor. Occasionally, despite all measures and healing at the fracture site, aseptic necrosis and degenerative changes began to show between one and one-half to two and one-half years. Experiments were started in 1940.

In the animal experiments[2] four objectives were sought: (*a*) a biologically inert material with suitable physical characteristics; (*b*) dispersion of stress to the host tissue; (*c*) undisturbed vascular supply, and (*d*) restoration and maintenance of form and function. Clinical application of the replacement principle brought in its wake many other considerations.

MATERIAL

Putti was one of the early modern surgeons to attempt arthroplasty or replacement. In his time the knowledge of the interaction of metals and tissue was rudimentary. Hey Groves experimented in various ways in joint restitution. Smith-Peterson, because of difficulties in using glass and Cellophane, settled on Vitallium.[3]

From the Surgical Division, St. Luke's Hospital.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 6, 1953.

1. Murray, C. R.: Unpublished data on muscle transplantations for delayed and non-union in fractures, the upper extremity of the femur.

2. Hudack, S. S.: Internal Prostheses for Injured Joints, New York, Boston, Philadelphia Fracture Day, Presbyterian Hospital (March 28) 1941.

3. Smith-Peterson, M. N.: Arthroplasty of the Hip: A New Method, J. Bone & Joint Surg. **21**:269-288 (April) 1939.

Venable and Stuck [4] and Hudack [5] brought some understanding to the behaviors of alloys in surgical use. Chrome-nickel-steel, reported on in its use in fracture surgery, was adapted to articular replacement.[6] But the idea of a fixed, yet adaptive, replacement element was difficult to establish because of the earlier teachings in cup arthroplasty. Harmon,[7] still working on cups, reported on the use of Lucite in a series of cases, and Judet and his associates [8] several years later also reported on acrylic arthroplasty but had adopted the adaptive fixation principle. The search for an ideal material for replacement elements continued [9] and still continues [10] in the studies of nylon, Kel-F, Saran, Vinyon, Orlon, Lucite, and Luxene (Table 1). There have been a host of surgeons who in episodic attempts have used many materials recently, too numerous to cite here. Despite the use of many varieties of articular replacements by surgeons, the basic problem of the ideal material still

TABLE 1.—*Comparison of Various Materials in Terms of Tissue Reaction, Electrolytic Activity, and Weight*

Material	Gross Tissue Reaction	Microscopic	Electrolytic	Source	Substance	Specific Gravity
Tantulum	30° unfavorable	Free particles	+ ±	.....	Tantulum TA 99.5%.....	16.6
Type 302 S.S.	30° unfavorable	Free particles	+ ±	Cu. 111	17-19 chrome 8-10 Ni.....	7.8
Type 9316 S.S.	10° unfavorable	Free particles	+	Ludlum	16-18 chrome 10-14 Ni 2-3 molybdenum	7.86
Stellite	No unfavorable	Fine crystals	±	Vitallium	Cobalt chrome molybdenum alloy	8.4
Lucite HC 202	3 mo. no unfavorable	Negative	0	DuPont	Methyl methacrylate HC 202	1.16
Nylon FM 10,001	3 mo. no unfavorable	Negative	0	DuPont	Polyamide Fl. 314.....	...
Nylon FM 3,001	3 mo. no unfavorable	6 mo. free particle reaction	0	DuPont	Polyamide 208.....	...
Kel-F No. 300	3 mo. no unfavorable	6 mo. negative	0	M. W. Kellog Co.	Polytrifluormonochlorethylene	2.1
Luxene No. 44	Unfavorable	Unfavorable	0	Luxene Co.	Copolymer methacrylate and vinyl acetate No. 44.....	1.19
Saran No. 517	Minimal	Minimal	0	Dow Chemical	Vinyl chr. and vinylidine chr.	1.68
Vinyon N NYGV	Minimal	Minimal	0	Union Carbon & Carbide	Acrylonitrile and vinyl chloride	1.68
Orlon	Minimal	Minimal	0	DuPont	Polyacrylonitrile	1.34

remains. The full understanding of the dispersal of stress to the host tissue is also far from complete, and clinical abuses and lack of understanding of a few basic requirements contribute to the chaos.

4. Venable, C. S., and Stuck, W. G.: Electrolysis Controlling Factor in Use of Metals in Treating Fractures, J. A. M. A. **111**:1349-1352 (Oct.) 1938.

5. Hudack, S. S.: High Chromium Low Nickel Steel in the Operative Fixation of Fractures, Arch. Surg. **40**:867-884 (May) 1940.

6. Hudack, S. S.: A Study in Articular Replacement, Ann. Surg. **124**:277-287 (Aug.) 1946.

7. Harmon, P. H.: Arthroplasty of the Hip for Osteoarthritis Utilizing Foreign-Body Cups of Plastic, Surg., Gynec. & Obst. **76**:347-365 (March) 1943.

8. Judet, J.; Judet, R.; Crepin, G., and Rigault, A.: Essais de prosthèse ostéo-articulaire, Presse méd. **55**:302 (May 3) 1947.

9. Hudack, S. S.; Blunt, J. W., and Darby, E. M. K.: A Study of Bone Matrix: The Application of Its Replacement with Artificial Substitutes, Am. J. Surg. **74**:579-585 (Nov.) 1947.

10. Blunt, J. W., Jr.; Hudack, S. S., and Murray, C. R.: Metals and Plastics in Orthopedic Surgery and General Surgery, read before the Thirty-Eighth Clinical Congress, American College of Surgeons, New York, Sept. 24, 1952.

DISPERSAL OF STRESS TO THE HOST TISSUE

The idea that with movement of the donor cup in cup arthroplasties no single area of the host bone is subjected to sufficient strain to cause local death is extremely attractive, but clinical application of the idea has shown it to be only partially and temporarily successful. Perhaps as the cup moved in the hip socket and was fixed to the neck a more stable equilibrium with the host tissue would be established. That was the hope. Certainly in the presence of inflammatory bone this is a false hope. Indeed, in five-year follow-up studies of replacements there is evidence that unless the tissue stress is dispersed more adequately than in the early type of

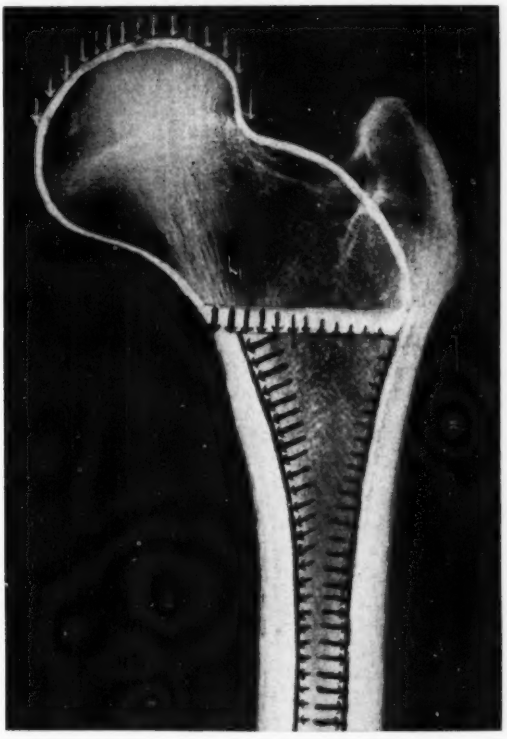


Fig. 1.—Maximum gross surface area for stress dispersion can be improved by threads, helical grooves, change of surface material and maximum adaptation to the optimum size of the intertrochanteric cone without weakening the cortex. Stress area in host tissue is outlined in black arrows.

replacement, absorption of the host bone and migration of the element takes place. Stress concentration, even in steel structures, will cause fatigue failure. It can cause fracture of plates and screws used in fracture fixation. On tissue, stress concentration causes tissue death and absorption. The design of a replacement element therefore demands that it should be applied with maximal dispersion of strain. For this reason maximum surface in the host tissue is a need (Fig. 1). No replacement element now in use fulfills that requirement completely. We sought to do this by providing a shelf rest at the plane of junction with tissue. The long

Fig. 2.—McBride replacement element. For purposes of clarity in reproduction the photograph of the element has been superimposed upon a photograph of the x-ray of a normal adult femur.

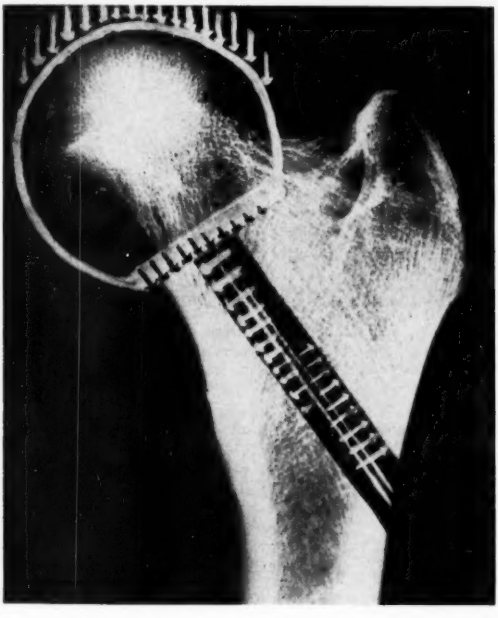


Fig. 3.—Roger Anderson element. Head portion is of nylon; shank, of stainless-steel tubing

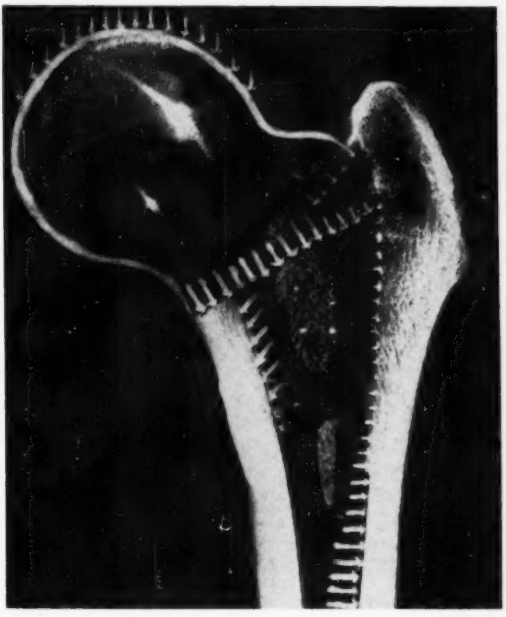


Fig. 4.—Austin Moore element. Maximum compression strain on host tissue is outlined in arrows.

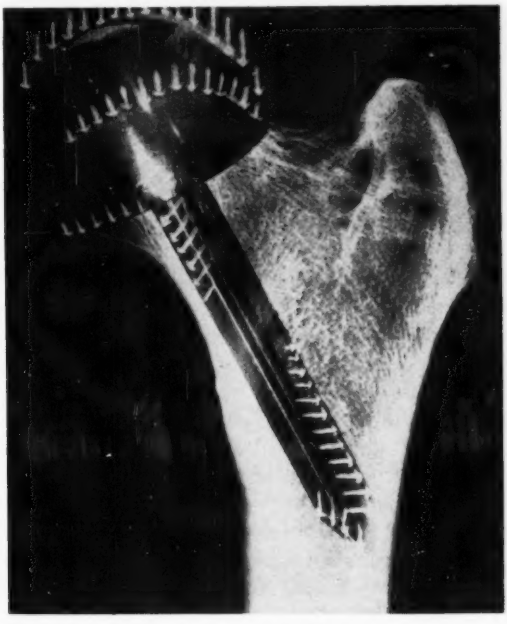


Fig. 5.—Judet element (metallic with flanged nail). Arrows in head portion outline the area of compression strain on the neck region of limited vascularity.

intramedullary parts of the shank were used to increase surface area. However, with a smooth metallic surface against tissue, there is little friction or tissue gripping. In the later models the steel surfaces were covered with nylon. To increase further the surface area dispersing the strain on the host tissue, the intramedullary portion was tooled with helical crossed coarse grooves. At present the McBride element comes closest to fulfilling this surface dispersion requirement but has other drawbacks. It may be necessary eventually to use a spongy or fibrillar nap similar to that in carpets to accomplish maximum dispersion of tissue stress. Certainly, it is not enough to have polished surfaces, as in the Anderson and other elements in which tubular or flanged pins are used. There is not enough increase in surface

Fig. 6.—Eicher element, heaviest of the elements considered.

area for host tissue contact to give validity to the designs. The most logical, though perhaps not most practicable, form for the fixing and dispersal part of the element is a truncated cone. The medullary canal is reamed to fit it. The region of flare going into the trochanteric enlargement seats the inverted cone to take care of pressure. The part fitting into the flared portion of the upper end should conform to the oval shape of the medullary canal for torque. The Austin Moore element has the nearest to adequate design as far as torque is concerned but falls short in other ways, such as the obliquity of the shelf, the lack of surface area for the host tissue. The Judet and Roger Anderson elements if seated at angles of more than 165 degrees weaken as far as torque strain is concerned. If they are applied at angles much less than 165 degrees, the torque strain is cared for, but the compression and shear strain of weight-bearing present problems which in long enough follow-ups will carry some of the compression strain to the surgeon himself. All of the metallic

elements have the fault that they are heavy. This may not seem important, but when one considers that each step constitutes a hammer blow to the host tissue, the weight of the hammer makes a big difference. From this viewpoint, the Anderson element, having a nylon head and a hollow steel tube stem, has virtue. It weighs about 3.5 oz. In comparison, the Eicher element weighs 16 oz.; the McBride, 12.5 oz.; the Austin Moore, 9.1 oz., and the metallic Judet, 4.2 oz. In general, the stainless-steel solid elements would be heaviest, the Vitallium castings next, and the plastic or plastic combined with metal the lightest. This may not appear to be an

Fig. 7.—C. R. Murray element. Development of the original elements for use in human beings was made possible by contract with the Office of Naval Research.

important consideration when the follow-up is only a few months or a few years, but will it mean the same in 10 or 20 years.

Fixation of the elements with screws or flanges connotes stress concentration until such time as the replacement element has equilibrium with the host tissue. Special fixation for torque, as in the McBride element, is contraindicated. For similar reasons the comparatively narrow dispersal which comes with the Roger Anderson and the Eicher elements is unphysiological. The cup portion of the Judet element is even less sound, both because of stress concentration at the cup margin and because of injury to the vascular supply to the supporting bone structure. Ideally, for stress dispersal the element should have maximum surface, step-cut,

serrated, or flanged seating in the inverted flattened cone between the trochanters. If the surface could be looped thread or filamentous nap of inert plastic with no water absorption to give maximum surface contact with the host tissue, then it would begin to approach the ideal. Even then it would have to be coarse enough to allow ingrowth and maturing of fibrous tissue. There are, however, many limitations in the structural reproductions of a gliding joint. The approach is mechanical and leaves unsolved many contingent problems in the hip joint. The limitation of time forbids any but the briefest consideration. How should clinical problems be attacked in which injury, degeneration, or tumor involve the pelvis as well? The molecular approach is ultimately necessary. With elastic sponge and fibrous plastics it may be possible to replace the joint entirely and increase the host tissue surface both in the pelvis and in the femur. This would make possible the excision and replacement of bone diseased of any cause. This is a very radical idea, but nature has already given us a guide in flail joints and pseudoarthroses.

VASCULAR SUPPLY

Whether in the healing of a fracture or successful articular replacement, the preservation of the blood supply of the host tissue is vital. We began replacement studies in the first place because blood supply to the head of the femur in high subcapital fractures was destroyed. When not destroyed, it was impaired enough to cause degeneration if not frank necrosis. The region of the femur best vascularized in the upper part is the intertrochanteric cortex. The poorest blood supply of the upper femur in the adult is the head and high neck. Any element which seats therefore on the intertrochanteric cortex has well-nourished host tissue. Those which seat above have poorly vascularized host tissue which is subject to absorption and degeneration. Anyone but the prejudiced user of cup arthroplasty must concede that the cup sits on a poorly vascularized neck and the rim of the cup, if mobile, goes banging down on what blood supply may be left as it comes up through the periosteal synovial reflexion on the neck. It is for the same reason that the Judet element can be dangerous to blood supply. Even with a flat shelf and a long intramedullary pin, when most of the stress was taken in the intertrochanteric area, resorption of bone can take place. When this bone is inflammatory, in addition, despite vascularity, it will not support the stress of weight-bearing on the element. It follows then that when the element is seated in well-vascularized bone the survival of the host tissue is more probable. Any replacement which sits high on the neck is on poorly vascularized bone and is unphysiologic. The Judet, the Eicher, and the Roger Anderson elements, the latter without compensating neck replacement collar, are less physiological than the McBride or the Austin Moore. Any element or application of it which requires excessive stripping with destruction of the periosteal blood supply is also unphysiologic. Ease of application and lack of stripping, as in a short-stemmed Judet, recommend it. However, there are other drawbacks, some already mentioned, which do not. It is manifestly impossible to consider here all the types of elements which are being used in various parts of the country and of the world. The number and variety of elements used is just a partial index of the chaos existing in this new field of restitutive surgery. One of the purposes of this paper then is to give, from our experience, a critical evaluation of the principles which must be fulfilled if a great deal of misdirected energy is to be channelized and perhaps a good deal of human misery prevented or alleviated. This brings us to the consideration of form and function.

MAINTENANCE OF RESTITUTION OF FORM AND FUNCTION

If the greater trochanter can be preserved intact and its muscle attachments uninjured, results are better. In hips with much fibrosis or deformation, the head may not be resected easily or even dislocated. With marked deformation it is necessary to detach the greater trochanter. In tumors and in traumatic or inflammatory destruction the greater trochanter and even part of the shaft may have to be sacrificed. Where possible, the attachment of the gluteii and small external rotators should be preserved. The integrity of the iliopsoas can be preserved and the rectus femoris reattached in the anterior approach. The posterior approach, on the other hand, forces the sectioning of the gluteus medius and sometimes part of the gluteus maximus and the gluteus minimus. The lateral approach lends itself poorly to access of the anterior and inferior acetabulum. In long-standing contractures an adductor tenotomy may be necessary to gain needed mobility for exposure and resection.

In deformity following fracture and nonunion, if the deformity is not too long-standing, normal form and length can be recovered. In one patient operated on five years ago we were able to recover 1½ in. (3.8 cm.) of shortening. There was gluteal pain for several months following operation. In hips which have much periarticular fibrosis or muscular contracture of long standing, obviously such restitution is impossible. The same is true in situations in which previous surgery and scarring are factors to be considered. There are many factors to be weighed in cases which depart from normal form. Thus in degenerative hips in which the head and acetabulum have been distorted or the neck deformed, restitution to normal form is out of question. The short broad neck, the flattened acetabulum, the long-standing external rotation and partial subluxation are only a few factors which influence the kinetic balance of the joint. These variations from the normal make it unwise to try for complete restitution of function and form. Obviously, in a patient who, because of pain or head and neck distortion, has shortening of the small rotators and the gluteus maximus, it will be difficult or impossible to restore a completely normal rotation gait.

In bilateral subluxating hips, where one side may have more dislocation and shallowness of the acetabulum, it is wise to consider a fusion on the one side. This is so not only because of muscle atrophy and shortening but also because the substance of the pelvis may not be deep enough to support the forming of a stable acetabulum without bone grafting to increase the acetabular shelf. In bilateral degenerative hips it is well to remember that the hip which has been deteriorating longer and has more atrophy of muscle, less motion, and perhaps less pain, will take much longer to recover than the other side, which has not stabilized. It may be a question of choice as to which side should be operated on first. Usually it is better to save the older stable hip and treat the still painful, more mobile, less degenerated hip. Not only does this give the patient a lift from relief of pain, but during convalescence the other hip is subject to more use and there is some recovery of muscle power as a result of the increased activity, which can speed its recovery when operated on.

Bilateral rheumatoid fused hips present a special problem. We do not know enough of the response of the rheumatoid hip to replacement to be sure that operating on them is completely justified. Let me cite two instances in which the patients had bilateral fusion. One patient has a five-year follow-up. His general disease is

TABLE 2.—*Sum*

Patient	Age, Yr.	Type of Replacement *	Surgeon	Condition	Approach	Date of Operation	Effectiveness of Surgical Replacement
M. B.	70	A. M.	S	Fracture cervical neck left femur	Posterolateral	8/ 2/52	Good
L. B.	47	A. M.	M	Fracture base left femur	.....	8/29/52	.....
M. B.	63	A. M.	D	Nonunion fracture neck left femur	.....	11/19/52	Difficult
C. B.	85	J.	B	Traction upper extremity of left femur	Anterior	3/12/51	Intermediate
O. B.	44	J.	D	Degenerative arthritis left hip	S. P. anterior	10/10/52	Good
G. B.	46	J.	M	Fracture upper extremity left femur	Anterior	4/25/51	Good
M. B.	57	A. M.	D	Ununited old fracture left femur	Posterolateral	4/30/52	Reamed acetabulum
W. C.	38	J.	B	Degenerative arthritis left hip	Anterior, rt. Anterior, lt.	12/29/51 2/ 5/52	Good Good
R. C.	53	J.	B	Malum coxae senilis right hip	Anterior	8/ 6/51	Good
C. C.	61	J.	D	Degenerative arthritis	Posterior	10/18/51	Good
M. D.	56	J.	D	Malum coxae senilis right hip	Posterolateral	6/20/52	Good
J. D.	66	J.	B	Malum coxae senilis right hip	Anterior	10/11/52	Good
M. D.	36	J.	B	Rheumatoid arthritis, bilateral right	Anterior	3/12/52	Good snug fit
M. D.	36	J.	B	Rheumatoid arthritis left hip	Anterolateral	3/24/52	Good snug fit
J. E.	78	R. A.	M	Subcapital fracture upper extremity right femur	Posterolateral	4/ 3/52	Good
G. F.	63	A. M.	M	Aseptic necrosis delayed ununited fracture right hip	Posterolateral	2/ 8/52	.....
C. F.	64	J.	M	Nonunion fracture neck of left femur	Anterior	6/29/51	Good
M. P.	65	J.	S	.....	.....	.....	.....
M. P.	65	J.	S	Malum coxae senilis right hip	Posterolateral	7/29/52	Adequate
M. G.	83	A. M.	D	Lorenzo lag screw; nonunion fracture neck of left femur	Posterolateral	3/28/52	Good
E. H.	92	M.	B	Fracture upper extremity intertrochanter of right remur	Anterior	9/29/52	Good
B. H.	75	A. M.	D	Nonunion fracture upper extremity of left femur	Posterolateral	4/28/52	Good
B. H.	66	J.	B	Aseptic necrosis of left femoral head	Anterior	10/ 3/51	Good
M. J.	49	J.	D	Degenerative arthritis hip bilateral; right fracture	Posterolateral, right	4/16/52	Good
S. J.	50	M.	B	Nonunion, left femur	.....	12/20/50	No record
G. J.	38	J.	M	Congenital dislocation	Posterolateral, right	4/29/52	Stable at operation
B. K.	61	A. M.	D	Nonunion upper extremity of left femur	Posteroanterior, left	9/29/52	Good, cane
L. L.	32	J.	B	Legg-Calvé-Perthes disease	Anterior, left	2/18/52	Fair
L. M.	93	A. M. M.	B	Intracapsular fracture upper extremity of right femur	Anterior	10/4/52 (A.M.) 10/8/52 (M.)	Unstable dislocation, 1st day postop.
Z. M.	54	E.	D	Nonunion fracture upper extremity of left femur	Anterior	8/27/51	Fair
F. M.	58	J.	D	Degenerative arthritis right hip	S. P. anterior	8/31/51	Good

Postoperative Fixation	Follow-Up				
No fixation	No active use	Cardiac decompensation	9/15/52, leg dangling	10/13/52, moves both feet	10/24/52, poor shuffle gait
.....	.....	.....	9/16/52, good motion	.....	9/20/52, smooth gait
Italic plastic boots	.....	Smooth course	12/5/52, flexion 124°	.....	12/17/52, walks with 2 canes
Buck's traction, 1 wk.	5/1/51, absorption	.....	5/21/51, slight walking	.....	.....
No fixation	No absorption	No undue pain	11/12/52, two canes	.....	.....
5/8/51, traction off	8/18/51, subluxation;	1/–/52, syphilis	10/15/51, cane	5/9/52, two blocks with canes	10/17/52, subluxation, ¾ in. shortening
.....	.....	.....	.....	.....	.....
Buck's extension, Wilke boots	.....	.....	2/25/52, walks unassisted	3/1/52, stairs with crutches	8/15/52, bilateral flexion, 90°
Traction suspension 10 days	8/20/51, active use and exercise	.....	.....	.....	8/27/51, crutch and cane 20 days postop.
.....	10/30/51, crutch walking	Severe intestinal ileus 5 days	11/6/51,, learning crutch walking	.....	11/11/51, crutch walking 3 wk.
Plaster boot, 1	Decubitus ulcers postop.	Decubitus ulcers postop.	9/19/52, crutch walking 3 mo.	11/7/52, two canes	1/9/53, two canes 7 mo.
.....	10/22/52, exercising	.....	12/19/52, walking with cane	1/9/53, pain and limit of abduction	11/14/52, discharged, walking with cane
Russell traction	4/7/52, patient on cast	4/30/52, 4 hr. barium retention	.....	.....	.....
Russell traction	4/7/52, knees most painful	Left foot drop	4/15/52, quadriceps not good, lt.	.....	5/3/52, stand and walk in walker
Plaster boot	5/20/52, able to walk; minor pain	5/3/52, soft tissue calcific	.....	.....	.....
2/15/52, balanced suspension	3/18/52,, no active motion	.....	.....	.....	.....
Wilke boots	.....	7/2/51, dislocation, posterior and lateral	8/22/51, removal of Judet	9/12/51, 2d stage osteomyelitis	.....
.....	.....	.....	.....	11/7/52, one cane	8/26/52, walks well with crutches
Balanced suspension	8/19/52, out of traction, patient doing well	Myocardial infarction	.....	.....	4/19/52, 50% range passive
Plaster boot	.....	.....	.....	.....	.....
Stable at operation	10/6/52, walker	Diabetes and hypertension	.....	.....	10/20/52, does well in walker
Stable at operation	6/20/52, walks poorly with crutches	.....	.....	.....	.....
Suspension 10 days postop.	10/16/52, sling exercises	.....	.....	11/2/52, active flexion 90°	11/9/52, cane and no limp
Single boot	5/13/52, standing on walker	.....	6/4/52, walks 100 ft. with crutches	.....	6/14/52, flexion to 84°, slow progress
.....	.....	.....	.....	.....	7/26/52, walks with crutches 70 yd.
Wilke boots	7/15/52, up in chair	.....	.....	.....	.....
Body cast	.....	.....	.....	.....	10/31/52, walks with 2 canes
Single boot	3/4/52, weight-bearing	.....	.....	.....	3/15/52, walks with 1 crutch
.....	10/16/52, died 8 days postop.	.....	.....	.....	.....
Wilke boots	9/16/51, boots off	9/17/51, resistive exercise	.....	.....	10/1/51, walks with 2 canes
Wilke boots	10/17/51, flexion 55°	10/29/51, flexion 70°	.....	.....	11/9/51, stairs and walking

TABLE 2.—*Summary*

Patient	Age, Yr.	Type of Replacement *	Surgeon	Condition	Approach	Date of Operation	Effectiveness of Surgical Replacement
L. M.	77	J.	D	Fracture upper extremity right femoral neck	Posterolateral	2/ 4/52	Fair
J. M.	64	J.	B	Post-traumatic arthritis	Anterior	12/15/52	Stable
M. N.	47	J.	B	Superior dislocation, subcapital fracture of neck of left femur	Posterior	5/ 9/52	Stable
P. O.	45	J.	B	Ankylosing spondylitis left hip	Anterior	12/21/51	Good, ease
B. P.	63	A. M.	M	Nonunion fracture neck of right femur	.....	5/12/52	.....
E. P.	71	A. M.	S	Nonunion fracture upper extremity of right femur	Posterolateral	2/ 9/52	Adequate
S. P.	35	A. M.	B	Legg-Calvé-Perthes disease, left hip	Anterior	11/22/52	Adequate
F. P.	57	J.	B	Malum coxae senilis, right hip	Anterior	3/ 7/52	Adequate
E. R.	56	J.	D	Nonunion fracture upper extremity of neck of right femur	Anterior	5/22/52	Fair
C. S.	76	J.	M	Degenerative arthritis right hip	Anterior	6/22/52	Fair
J. S.	86	J.	B	Subcapital fracture upper extremity of right femur	Anterior, poor operative risk	6/24/52	.....
C. S.	62	J.	D	Degenerative arthritis left hip	Anterior	4/ 9/51	Difficult excision
C. S.	46	R. A. (rt.) A. M. (lt.)	M	Rheumatoid arthritis bilateral	.....	8/12/52 9/ 9/52	.....
R. S.	54	J.	D	Degenerative arthritis right hip	Posterolateral	5/19/52	.....
I. S.	69	A. M.	D	Nonunion fracture upper extremity of right femur	Anterior	11/ 3/52	Difficult
V. S.	46	J.	D	Degenerative arthritis right hip	Posterolateral	8/26/52	Adequate
N. S.	49	E.	D	Nonunion fracture upper extremity of left femur	Anterior	9/11/51	Fair
S. T.	27	J.	B	Rheumatoid arthritis left hip	Anterior	7/24/52	Difficult
E. W.	41	R. A.	M	Ankylosing hip, left	.....	11/19/52	Adequate
J. W.	65	J.	D	Degenerative arthritis left hip	Anterior	8/16/51	Good
D. S.	38	O. N. R.	H	Chondrosarcoma right	Anterior	1/—/47	Difficult
J. A.	28	O. N. R.	H	Chondrosarcoma right	Anterior	10/ 7/49	Difficult
D. B.	54	O. N. R.	H	Degenerative arthritis right hip	Anterior	11/20/47	Fair
J. G.	30	O. N. R.	H	Rheumatoid arthritis bilateral fusion	Anterior	1/15/48 (rt.) 4/12/48 (lt.)	Good
D. S.	64	O. N. R.	H	Aseptic necrosis fracture upper extremity of left femur	Anterior	2/29/48	Good
N. M.	28	O. N. R.	H	Osteomyelitis	Anterior	.....	.....
J. S.	34	O. N. R.	H	Chondrodysplasia	Anterior	3/—/48	Dislocation unstable
J. R.	36	O. N. R.	H	Bilateral dislocation	Anterior	4/—/48	Good
T. R.	38	O. N. R.	H	Aseptic necrosis bilateral	Anterior	6/—/48 12/—/48	Good
H. J.	32	O. N. R.	H	Degenerative arthritis	Anterior	3/—/48	Good
A. S.	34	O. N. R.	H	Rheumatoid arthritis	Anterior	—/—/48	Good
E. C.	36	O. N. R.	H	Degenerative arthritis	Anterior	5/—/49	Good

* The following abbreviations are used: A. M., Austin Moore; J., Judet; R. A., Roger Anderson; M., McBride; E., Eicher; O. N. R., Official Naval Reserve.

Postoperative Fixation	Follow-Up				
Plaster boot	2/18/52, able to move leg	.....	.....	.....	2/27/51, full weight-bearing in walker
Balanced suspension	12/26/52, sling motions	1/1/53, superficial drainage	.....	.....	1/6/53, flexion 85°, walks with crutches
Cast	6/13/52, crutch walking, in cast	.....	.....	.....	6/21/52, discharged with cast
Snug balanced suspension	1/8/52, stood today	.....	1/12/52, up on crutches	.....	1/19/52, one cane, flexion 68°
Cast	6/2/52, muscle setting	6/6/52, walking strolling gait	CVA several yr. ago	.....	6/7/52, walking with help
.....	2/23/52, out of bed with foot drop brace	.....	2/26/52, up in walker	.....	3/25/52, walking; weight-bearing
Balanced suspension	12/8/52, rt. traction in abduction	12/15/52, ambulation	12/22/52, flexion 60°, abduction 45°	12/24/52, flexion 120°, abduction 180°	1/21/53, poor walking, old poliomyelitis
Traction abduction	3/20/52, up in walker	.....	.....	.....	3/29/52, walks with 1 cane
Wilke boots	6/3/52, abduction suspension	6/4/52, non-hemolytic Strep.	6/18/52, walking training	.....	7/3/51, progress satisfactory
Balanced suspension	.....	.....	.....	7/8/51, non-weight-bearing cruteh	7/20/51, uncooperative patient
Plaster boot, rt.	.....	6/25/52, died, 1st postop. day	.....	.....	.....
Stable	4/21/51, manages crutches well	.....	.....	.....	5/8/51, walks with 1 cruteh
.....	Nonhemolytic Strep., lt.	.....	.....	.....	11/14/52, stood poorly; 3/13/52, one cruteh, includes stairs
Plaster boot, rt.	.....	11/5/52, distortion	12/12/52, good function	12/21/52, stable hip	12/30/52, walks with 2 canes
Wilke boots	.....	.....	9/9/52, flexion 29°	.....	9/15/52, walked once
Plaster boot, rt.	.....	.....	.....	.....	.....
Wilke boots	Improved in past 1 yr.; virtually full motion	7/4/52, slight limit of abduction; pain	10/5/51, flexion 92°, abduction 48°	10/24/51, flexion 115°, abduction 45°	11/9/51, some limp on cane
Balanced suspension	8/16/52, flexion 120°	8/20/52, flexion 110°, walks well with cane	Posture improving	.....	8/20/52, flexion 100°, ambulatory with cane
Body cast	12/14/52, dangle in bed	.....	.....	.....	1/21/53, walking with cane
Traction suspension	.....	9/4/51, dislocation reduced	.....	.....	9/21/51, gait fair, walker
Plaster spica	.....	.....	10/1/48, no pain, no cruteh	7/31/49, uses 2 crutches	7/31/50, died
Plaster spica	.....	.....	.....	.....	2/9/53, going to to school; pain; drives car
Spica	.....	.....	10/10/48, works farm, 1 cruteh	10/9/52, removal of element	2/7/50, works on farm
Traction suspension	.....	.....	10/10/48, confined to bed	.....	2/5/53, confined to bed
Traction suspension	.....	.....	10/1/48, very little pain	2/16/53, walks with cane	Housewife; 1 cane
Spica	.....	6/-/51, removal of element	1 yr. postop., 2 crutches	2 yr. postop., pain and absorption	Fused; no pain; walks with 2 crutches
.....	.....	.....	1 yr. postop., no support	2 yr. postop., drives car, pain	Electrical appliances
Spica	.....	.....	1 yr. postop., 1 cane	Housewife; no pain	2/5/53, drives car; wants to walk
Spica once; dislocation once	.....	.....	1 yr. postop., 2 canes	.....	Engineer with Dept. 720; 2 canes
Spica, dislocation	.....	.....	.....	.....	Radio repair; 1 cane
Traction suspension	.....	.....	1 yr. postop., walks with cruteh	2 yr. postop., uses 2 crutches	Optical shop
Traction suspension	.....	.....	1 yr. postop., walks with crutches	.....	.....

so severe that he is confined to bed most of the time. There is some squeaking of the joints but no pain. The motion is about what it was five years ago. The other patient was operated on more recently, with a follow-up of not quite five years. He had been in bed for nine years before surgery. Since then he has been married and runs an optical shop. He can ride in a car and negotiate stairs but his mobility is not particularly good. Until we know more of the rheumatoid process and how to control it, we are very circumspect in attacking this problem. Like all other lesions, it must be evaluated on the merits and pitfalls inherent in each case and judged so. The temptation to help, especially in a losing battle, is great, but perhaps the most help can be given in cases in which the fight is lost and the process is "burnt out." At least in these instances there is no other possibility than improvement. Where many other joints are active and there is much pain or advanced parenchymatous disease of vital organs, the risk is, of course, greater and the potential benefit less.

CLINICAL DATA

This critique is based on 63 cases and 66 (Table 2) operations done by five operators. In 51 cases the operations were done at St. Luke's hospital, Cleveland. The other operations were performed at Presbyterian Hospital, New York. Of the types of elements used, there were 31 Judet, 14 Austin Moore, 14 C. R. Murray, 4 McBride, and 1 Eicher. The oldest patient was 92 years of age, the youngest 28.

The types of cases were as follows: fracture of the upper extremity of the femur with nonunion or aseptic necrosis, 25 cases; degenerative arthritis and malum coxae senilis, 18 cases; rheumatoid arthritis, 8 cases; congenitally dislocating hips, 2 cases; traumatic dislocation, 1 case; chondrosarcoma, 2 cases; osteomyelitis, 1 case, osteochondrosis of capital epiphysis of femur (Legg-Calvé-Perthes disease), 2 cases; chondrodysplasia, 1 case, and post-traumatic degeneration, 2 cases.

The posterolateral approach was used 17 times, the anterior approach 47 times. Four dislocations occurred, three in anterior approaches. The postoperative fixation varied from a single boot to limit rotation, through Wilkie boots and body spica, and from no fixation through Russell traction, Buck's extension, balanced suspension, and traction suspension. The complications included two myocardial infarctions, three infections (one preoperative), one acute gall bladder disease, severe intestinal ileus, cardiac decompensation and foot drop, and one operative death, that of an 86-year-old patient, a known operative risk. The follow-ups extend from a few months to five years, the majority being between one and two years.

COMMENT

From this experience, we can say that no articular replacement will give a normal hip joint. The patient should be warned that he will never regain a vigorous or unlimited use. If the pain is severe or the limitation of motion marked, operation is indicated. In subcapital fractures with nonunion, aseptic necrosis, or degeneration, each case should be considered individually. Accurate x-ray measurements should be made and when possible the replacement elements made to fit the patient. We avoid the indiscriminate use of the mass-produced element which may have as the chief recommendation the fact that it is cheaper than another. The problem of joint replacement should be seen and critically evaluated as a special application of restitutive principles in general surgery. Errors which in long-term follow-up may lend a bad aura and prejudice the future development of restitutive surgery must be understood and shunned. Indication for the use of replacement should be clear. Contraindications should be clearer still (Table 3).

TABLE 3.—*Indications and Contraindications for Use and Rejection of Articular Replacements**

Indications for Use
Aseptic necrosis of head of femur, post-traumatic or fracture
Nonunion of neck of femur with absorption deformation and pain
Severe degenerative arthritis, pain limitation of motion, contracture
Tumors, benign and limited malignant growth
Congenital dislocations, bilateral, with pain, degeneration, contracture, severe disability
Certain rheumatoids ? arrested, limited general disease
Contraindications
Infection, acute and chronic, osteomyelitis, hematogenus or post-traumatic
Physiologic incompatibility of host bone
Metastatic tumors
Osteolytic malignant tumors
Paget's disease
Inflammatory lesions of bone in general
Vascular disease of bone, osteoporosis, Sudeck's caisson disease
Rheumatoid activity, multiple involvement, parenchymatous disease
Status of patient, general debility, intercurrent disease, severe metabolic disturbances

* The merits of the individual case to justify the ultimate decision.

CONCLUSIONS

No replacement element now in use fulfills all the physiological requirements. Dispersal of strain on the host tissue can be improved. Replacement elements must be made lighter. Experiments in the search for an ideal plastic should be continued. Clinical indications for use of the replacement principle should be narrowed. Abuses of the replacement principle which may prejudice the development of restitutive surgery are to be measured and avoided.

DISCUSSION

DR. GEORGE J. CURRY, Flint, Mich.: It is certainly refreshing to have an investigative brain of the type of Steve Hudack's. There are not too many persons like that in the world right now. He is an investigating surgeon, and it has been my pleasure to have known him since 1939, when he referred to the late Clay Ray Murray and the remarks he (Murray) made relative to progress.

I should like to ask you, Dr. Hudack, what the reactions are in a hip joint in which there is a metallic replacement?

I should like also to ask what the reactions are in the medullary canal with the use of those units that project into it?

What is your opinion as to whether or not there should be an operation of election for the femoral neck fractures in elderly patients, in whom there is the one chance in five of necrosis, an avascular necrosis?

You referred to these 38 different replacements, but you did not say which one you thought could not take in the first place. May I have your comments?

DR. S. S. HUDACK, Cleveland: We have had one death from tumor in a five-year follow-up group and a specimen, which I do not have with me, of a tumor from a 6-year-old dog.

As to the subchondral reaction, there was a little subchondral increase in density; consequently, there was greater subchondral support. There is periosteal and subperiosteal proliferation, as there would be in long-standing intramedullary fixations. The lone intramedullary pins were used in the early models, and these are now discarded.

As an elective procedure, I think it depends entirely on the surgeon whether or not he undertakes to do it in a patient such as a 75-year-old woman with a hip fracture who will probably die otherwise, or if pinning is done, will live on to experience necrosis. If he has the background and the backing of his staff, and the support of the community, I think he could do it as an elective procedure.

No prosthesis is available at present that absolutely answers all the desired criteria. I should like to show you one of the later ones that we used. We are still working on that problem. We "tailor up" the ones we use to the needs of the patient.

CARDIAC ARREST

Its Prevention and Treatment

EGBERT H. FELL, M.D.

LOWELL F. PETERSON, M.D.

AND

NEWTON CHUN, M.D.

CHICAGO

THE MEDICAL literature [1] gives a good review of the history concerning the problem of cardiac arrest, its causes, recognition, and the various methods of therapy. The importance of various drugs, methods of administration, and differences in opinions concerning the dosages are of interest. Much time is spent on the active therapy in producing an artificial circulation, and the importance of starting this within a minute to three minutes after arrest is usually emphasized. The terminology for this artificial circulation may be cardiac massage or cardiac compression. The latter term, we believe, is preferred because it more clearly describes what is necessary to maintain an artificial circulation. Authors are now emphasizing that the most important factor in the prevention and cure of the catastrophe is an open airway which delivers oxygen and takes away the waste products, this being essential for a good respiration. Furthermore, surgeons and anesthetists are realizing the importance of keeping the anesthetic agents as simple and as minimal as possible.

From the Rush Laboratories of Presbyterian Hospital.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 6, 1953.

1. Ehrenhaft, J. L.; Eastwood, D. W., and Morris, L. E.: Analysis of 27 Cases of Acute Cardiac Arrest, J. Thoracic Surg. **22**:592 (Dec.) 1951. Bailey, C. P., in discussion on Ehrenhaft and others. Birnbaum, G. L.: Simple Cardiac Defibrillator, J. Thoracic Surg. **23**:183 (Feb.) 1952. Björk, V. O.: Circulatory Arrest, ibid. **24**:611 (Dec.) 1952. Dale, W. A.: Cardiac Arrest: Review and Report of 12 Cases, Ann. Surg. **135**:376 (March) 1952. Gordon, J. N.; Sternlicht, I. R., and Weaver, O. M.: Personality Changes Following Cardiac Arrest, U. S. Armed Forces M. J. **3**:1411 (Oct.) 1952; Abstracted J. A. M. A. **151**:78 (Jan. 3) 1953. Harken, D. E., in discussion on Ehrenhaft and others. Hurwitt, E. S., and Seidenberg, B.: Rupture of the Heart During Cardiac Massage, Ann. Surg. **137**:115 (Jan.) 1953. Johnson, J., and Kirby, C. K.: The Surgical Treatment of Ventricular Fibrillation, ibid. **134**:672 (Oct.) 1951. Johnson, J., in discussion on Ehrenhaft and others. Kay, J. H.: The Treatment of Cardiac Arrest: An Experimental Study, Surg., Gynec. & Obst. **93**:682 (Dec.) 1951. Kay, J. H., and Blalock, A.: The Use of Calcium Chloride in the Treatment of Cardiac Arrest in Patients, ibid. **93**:97 (July) 1951. Mackay, R. S., Mooslin, K. E., and Leeds, S. E.: The Effects of Electric Currents on the Canine Heart with Particular Reference to Ventricular Fibrillation, Ann. Surg. **134**:173 (Aug.) 1951. Overholt, R. H., in discussion on Ehrenhaft and others. Potts, W., in discussion on Ehrenhaft and others. Reid, L. C., Stephenson, H. E. Jr., and Hinton, J. W.: Cardiac Arrest, A. M. A. Arch. Surg. **64**:409 (April) 1952.

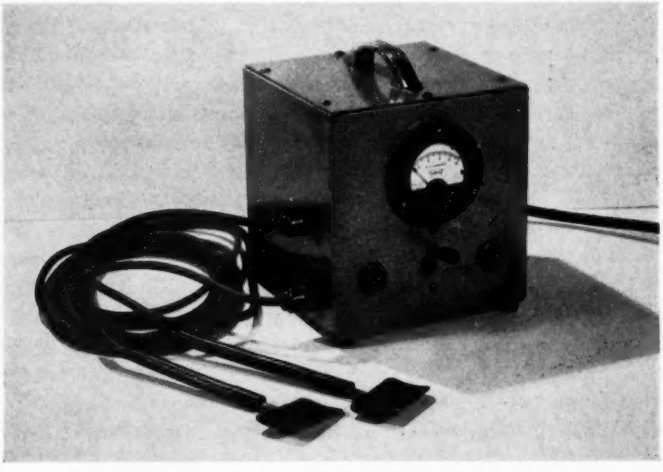
This problem is one for the anesthetist and surgeon, and together they should study every possible means of prevention of this entity that formerly was relegated to the diagnosis of "death due to undetermined origin," "cardiac death," "anesthesia death," "thymic death," etc. Most surgeons know that cardiac arrest may occur yet have not recognized it, nor would they know how to handle such a situation if it did occur. Neither do they realize that together with the anesthetist they are frequently responsible for the prevention or the development of an arrest.

The purpose of this paper is to encourage each surgical and anesthetic department, regardless of size or location, to develop together their skills in the dog laboratories for the prevention, recognition, and treatment of this emergency. Most hospitals do not have an organized dog laboratory, but one can easily be set up for this important problem. Dogs can be purchased or obtained from the city dog pound, and put to sleep by means of intravenous injections of pentobarbital (Nembutal). Intratracheal intubation of the dog is essential, and, after the chest is opened, positive pressure is maintained by the anesthetist. For demonstration purposes a midline sternal incision is best. The pericardium is opened, completely exposing the heart and region of the great vessels. The anesthetist will now play the important part in the demonstration. Attention is called to the free airway and the bright-red color of the blood and the well-oxygenated appearance of the cardiac muscle, the lungs, and other tissues. Various methods of producing obstruction to the free exchange of oxygen can then be tried, showing how easily and rapidly cyanosis and cardiac irregularities develop. When the tracheal catheter is completely occluded, the heart rate speeds up, cyanosis develops, the heart dilates and slows. One marvels that the heart does not rupture, it becomes so distended and cyanotic. If at this time the airway is opened and oxygen is delivered to the lungs, a dramatic response is seen. The heart receives oxygen, and at once it renews its work with great vigor; cyanosis clears and the heart size returns to normal. The importance of this open airway and of oxygen to the cyanotic dilated heart that is at the point of arrest has been most beautifully shown. The airway, again, should then be completely closed off, allowing at this time the heart to pass through the above stages to a complete arrest. The heart will be markedly dilated, cyanotic, and without contraction. When allowed to stay in this condition one-half to one minute, an open airway may not be sufficient to resuscitate the heart action. Manual compression of the heart should then be started, completely emptying the heart by forcefully compressing the heart and then releasing it, thus allowing the heart to refill. Just as soon as it refills to normal size, rapid vigorous compression should be repeated. Systole and diastole must be continued by compression and relaxation of the hand or hands so that good color returns to the tissues and a pulse can be felt in the peripheral vessels. The arrest may be overcome in two or three compressions, or a considerable length of time may be required to restore cardiac rhythm.

Careful observation of the cardiac muscle is essential to differentiate between complete cardiac arrest and ventricular fibrillation. The appearance of the fibrillating ventricles has been described in various ways: worm-like motion of the muscles, no uniform motion of the ventricles, independent motion of each muscle bundle, so that no function of the ventricles occurs. When fibrillating ventricles are seen,

cardiac compression must be instituted until the defibrillator is ready to function. (A defibrillator should be a part of the emergency equipment of each surgical department.)

Ventricular fibrillation may not occur after this above experiment, and, in our experience, a severe electric shock is required to cause the heart to go into ventricular fibrillation. This shock is produced by clamping one electrode to the neck and the other to the groin of the dog and allowing the electric current received from a wall plug to pass through the dog. Two or three shocks may be necessary in the larger dogs to produce fibrillating ventricles. When this occurs, it is easily seen that the heart is not functioning, yet all muscle fibers are in motion. There is



Photograph of a defibrillator which was made at the cost of $32.00 by Dr. Donald Fisher. He followed the advice and designs recorded by Mackay and his associates in the August, 1951, issue of the *Annals of Surgery*. This instrument has proved its value many times in the dog laboratory, and it has been used to defibrillate the heart of a human being.

no pulse beat and no heart sounds, and only direct vision or an electrocardiogram can be used in making the diagnosis. The heart distends and becomes very cyanotic and, except for the fibrillating muscle, appears like the heart in complete arrest. Manual compression of the heart is essential for oxygenation of the heart and brain, and, when the heart muscle is well oxygenated, the defibrillator should then be used. The dog laboratory is the place to acquaint the house and attending staffs with the technique and dangers of this instrument, as well as to realize that it may take considerable time and effort to accomplish defibrillation.

SUMMARY AND CONCLUSIONS

Cardiac resuscitation is only possible if one is able to recognize a cardiac arrest and institute a bold well-organized plan. The animal laboratory is invaluable in this training program.

The most important lesson to be learned in this demonstration, both for the anesthetist and surgeon, is the realization of the importance of an open airway in the prevention of this catastrophe.

DISCUSSION

DR. JACOB K. BERMAN, Indianapolis: I do not believe that this splendid paper should go without some comment, and I rise to reemphasize a few physiological principles which perhaps all of you know but which have recently been rediscovered in our laboratory.

Carotid body reflexes are not concerned with respiration in normal circumstances. It is only in severe degrees of oxygen lack or carbon dioxide excess that its chemical receptors furnish afferent impulses which keep the respiratory center active.

The respiratory center is stimulated primarily by carbon dioxide and not by oxygen lack.

The carotid body is affected predominantly by oxygen lack and not by carbon dioxide excess, unless extreme. Indeed, its receptor cells are probably the only cells in the body that are stimulated to any degree by oxygen lack. All other cells are depressed. Narcotic drugs, barbiturates, and deep anesthesia interfere with the response of the respiratory center to chemical changes, but reflexes from the carotid body are much less affected.

During anesthesia, oxygen is usually given, thereby lulling the carotid body into a sense of security; moreover, its receptors are much less sensitive to carbon dioxide increase than to oxygen lack. In the experimental animal, four times the volume of carbon dioxide is required to cause reflex hyperpnea through the carotid body than by direct effect on the respiratory center.

The conclusions are obvious. When the respiratory center is greatly depressed by large doses of morphine, barbiturates, alcohol, or by deep anesthesia, it will not respond to its normal stimulus, carbon dioxide. The carotid body takes over, but its receptors are influenced more by oxygen lack, which may not be severe, than by carbon dioxide excess. Therefore the effects of carbon dioxide stimulation on the respiratory, cardiac, and vasomotor centers will not be apparent to the anesthetist until hypercapnia is dangerously high.

Dr. Fell and his associates have outlined and beautifully illustrated the relatively simple measures which will usually avert disaster when the patient is under anesthesia. They may be summarized as follows: (1) the cautious use of drugs and anesthetic agents which greatly depress the medullary centers, and (2) maintenance of an open airway at all times, with an adequate supply of oxygen and ample provision for the removal of carbon dioxide.

DR. GEORGE H. A. CLOWES JR., Cleveland: I should like to second Dr. Berman and to complement Dr. Fell on this beautiful movie and on his emphasis to all of us about the importance of the recognition of this problem.

I should also like to emphasize another point that seconds what Dr. Berman has said—that this is not a function of the heart alone. It is a function of the central nervous system and the heart. I should like to tell a short story to illustrate this.

In operating on a child with a tetralogy, we reached the point where we were about ready to do an anastomosis. The whole situation seemed bad, and there was not much we could do to improve this child's respiration. At that time one of us remarked, "Now, if we can get through this thing in 15 minutes or so, everything will be all right."

About that time, the heart began to slow down. Presently, as we watched it, it went into arrest, then fibrillated. This all took place rather faster than it takes to tell.

We were faced with what looked like a desperate situation, with no way of improving the circulation and no way of improving the respiration beyond what the anesthetist was doing. We were able to keep the circulation going, naturally, by cardiac massage.

We gave the child a large dose of atropine—which, of course, had been done preoperatively. We administered 0.03 mg. of atropine, and much to our delight, after further massage, we were able to defibrillate this heart.

I only mention this to emphasize again that this is a combined function. In this particular instance, we blocked the vagus nerve, transmitting its impulses from the central nervous system.

DR. J. L. EHRENHAFT, Iowa City: I should like to point out a few things learned from experiments carried out in the production of cardiac arrest in dogs about two or three years ago.

If adequate artificial circulation and ventilation with oxygen are provided for the animal that has had a cardiac arrest, the peripheral arterial blood levels of oxygen and carbon dioxide can be maintained well within normal limits. The carbon dioxide may be even lower than normal levels, since it can be easily blown off by overventilation if an effective circulation is maintained.

I think one of the most important points is not to waste any time between recognition of defective circulation in cardiac arrest and the application of corrective measures.

Only recently—about two weeks ago—we had a patient whose heart we massaged for 1 hour 20 minutes; she was a postpneumonectomy tuberculous patient, and the condition was hopeless, we thought, but the woman survived. She has some cerebral damage but is improving.

One should never give up, particularly in young people with relatively normal hearts. Of course, this is not always true in the older age groups.

SURGICAL TREATMENT OF THE CONGENITAL FUNNEL-CHEST DEFORMITY

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AND
GEORGE L. EMERSON, M.D.
ROCHESTER, N. Y.

THE CONGENITAL funnel-chest deformity has been recognized for many years, but its adequate surgical correction is a relatively recent development. The historical aspects of our knowledge concerning this condition have been admirably summarized by Ochsner and DeBakey,[1] and more recent reports have led to the present-day understanding of the essential features of the deformity. The purpose of this report is to consider the lessons which we have learned in the management of 18 patients during the past five years. At the beginning of our experience the indications for operation were not completely clear, the optimal time for operation was not well established and there was no uniformity of opinion as to the extent of operative procedure necessary in the various age groups. We now feel that the optimum age for the operation is about 5 years and reserve the limited operation of Brown[2] for infants who are having severe symptoms as a result of the deformity.

The deformity has been described by a variety of terms such as *Trichterbrust*, koilosternia, pectus excavatum, and chonechondrosternon. The term funnel chest is now most commonly used, and this describes very adequately the gross appearance of the chest wall. The condition is characterized by a posterior depression of the sternum which begins at the junction of manubrium and gladiolus and increases to the point of maximal displacement at the junction of the gladiolus and xiphoid. The xiphoid is usually angulated acutely anteriorly. There is angulation of the costochondral junctions in such a manner that the sternal ends of the cartilages are elongated and sharply depressed in a posterior direction. The deformity varies in its external configuration. There may be a narrow inverted cone or funnel-shaped deformity which involves only the sternum and costal cartilages and whose apex

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Instructor in Surgery (Dr. Emerson).

Associate Professor of Surgery (Dr. Mahoney).

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 6, 1953.

From the Department of Surgery, University of Rochester School of Medicine and Dentistry, and the Surgical Service of the Strong Memorial and Municipal Hospitals.

1. Ochsner, A., and DeBakey, M.: Chone-Chondrosternon: Report of a Case and Review of the Literature, J. Thoracic Surg. **8**:469, 1939.

2. Brown, A. L.: Pectus Excavatum (Funnel Chest) Anatomic Basis: Surgical Treatment of the Incipient Stage in Infancy and Correction of the Deformity in Fully Developed Stage, J. Thoracic Surg. **9**:164, 1939.

may be in the midline or eccentrically placed. The deformity may at times be broad and flat with depression of the ribs at the level of the xiphoid as far laterally as the nipple line with flaring of the costal margin.

The cause of the deformity is not well understood. Many theories have been suggested, such as fetal position in utero, upper respiratory tract obstruction, and others,[1] but none of these adequately explain the origin of the condition. There is a tendency for it to occur in succeeding generations of a family, but in many instances there is no family history. Only 2 of our 18 patients have a positive family history. The condition also may be associated with other congenital defects, but in a high percentage of cases it is the only defect. Two of our patients had Marfan's syndrome. The primary defect seems to be maldevelepoment of the anterior musculature of the diaphragm with a shortening of the central tendon which causes an unnatural pull on the sternum and lower ribs. Brown [2] has pointed out that there is also a thickening of the substernal ligament, i. e., the attachment of the linea alba, at the lower end of the body of the sternum. Lindskog and Felton [3] have termed this situation a muscular skeletal imbalance. When one considers the characteristics of the deformity, it seems logical that abnormal pull of the diaphragm is of utmost importance.

Figures 1 and 2 indicate our interpretation of the two types of the deformity which we have termed the "narrow" and the "broad." Evans [4] has grouped his patients according to three categories: the funnel, the cup, and the saucer. The narrow deformity (Fig. 1) is characterized by a thickened tense substernal ligament and a shortening (or muscular imbalance) of the central attachment of the diaphragm to the lower end of the sternum. The broad type has, in addition to the above, a shortening of the more lateral anterior attachments of the diaphragm which exerts tension through its attachment to the lower ribs. This causes the depression of the ribs laterally as far as the nipple or anterior axillary line and retraction of the sternum with inspiration. A proper understanding of these attachments is necessary in planning the operation for correction of the deformity.

There are secondary abnormalities resulting from this condition other than the obvious deformity. The posterior displacement of the sternum results in an oblique angulation of the ribs which is obvious by x-ray examination and results in a long narrow chest.[5] The shoulders are held high and forward, resulting in a stooped round-shouldered appearance. There is a tendency to an increase in the normal dorsal kyphosis and the abdomen is protuberant. The heart is usually displaced to the left but may be compressed by the sternum in the midline or may be angulated to the right side. The paradoxical movement of the chest, i. e., marked retraction with inspiration, is a most striking feature in infants and in young children.

The indications for operative correction vary according to the symptoms which are present and with the severity of the deformity. The most prominent symptoms in infancy are respiratory and gastrointestinal. Six of our patients were operated upon before the age of 15 months and all had respiratory symptoms. Noisy sterterous respiration (especially when sleeping) was present in all. They all had

3. Lindskog, G. E., and Felton, W. L., II: Pectus Excavatum: A Report of 8 Cases with Surgical Correction, Surg., Gynec. & Obst. **95**:615, 1952.

4. Evans, W.: The Heart in Sternal Depression, Brit. Heart J. **8**:162, 1946.

5. Teplick, J. G., and Drake, E. H.: Roentgen and Cardiac Manifestations of Funnel Chest, Am. J. Roentgenol. **56**:721, 1946.

frequent persistent respiratory infections, usually associated with croup. This group also tended to be underweight, and they were usually feeding problems. One patient (S. S.) had vomited persistently since birth, requiring thickened feedings and antispasmodic drugs. The vomiting was such a prominent feature that careful

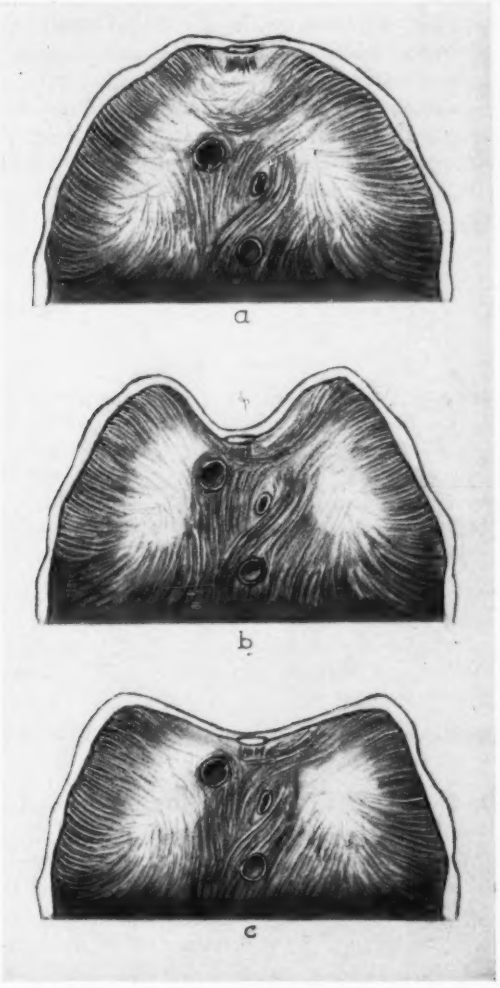

Fig. 1.—Schematic diagram of (*b*) the shortening of the central anterior portion of the diaphragm in the narrow deformity and (*c*) the wider area of shortening in the broad deformity.

gastrointestinal studies were performed before operation to rule out a partial congenital bowel obstruction. Immediately after division of the attachments to the sternum, the baby's respirations imrpoved and he had no further feeding difficulties. These infants are apparently exerting a strenuous effort to breathe, and this

is reflected in symptoms of other organ systems. It should be emphasized that the patients must have a thorough investigation of their respiratory tract to rule out obstruction to the airway.

The symptoms produced by the deformity in older children are usually not severe, but the deformity increases. As the patient reaches adolescence or young adult life, a variety of conditions may develop. The cardiac symptoms have frequently been emphasized, and these may be of a serious nature. Palpitation, dyspnea with exertion, precordial pain, and tachycardia may develop. Dorner and his associates [6] have reported on a 28-year-old man who had an abnormal angiocardiogram with puddling of dye in the right atrium and distortion of the tricuspid valve. Operative correction of the deformity resulted in relief of symptoms and in a normal angiocardiogram. Lindskog and Felton [3] have reported abnormal cardiac catherterization findings in these patients, and Ravitch [7] has reported frank congestive failure relieved by operation. We have a 16-year-old boy whose heart is so

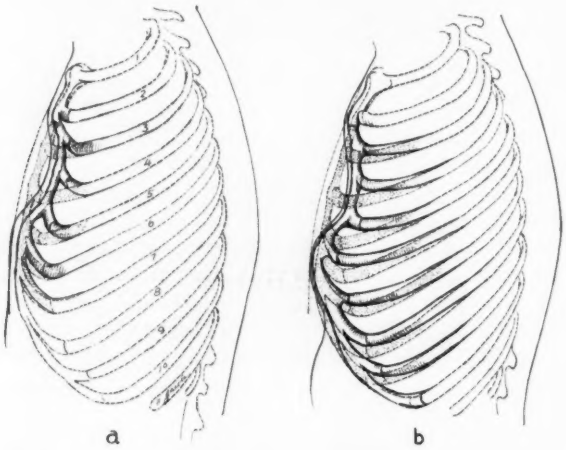

Fig. 2.—Angulation of the costochondral junctions in (*a*) the narrow deformity and (*b*) the broad deformity.

compressed by the sternum that it produces adventitious heart sounds and severe pain with exertion. Evans [4] has pointed out an interesting group of patients who did not have cardiac symptoms but in whom the deformity produced apparent abnormalities which led their physicians to believe they had heart disease. The signs which had been erroneously misinterpreted were systolic murmurs and apparent cardiac enlargement because of the displacement of the heart from behind the sternum to the left.

The symptoms other than cardiac may not be so striking, but they are of importance in the life of the patient. The exercise tolerance is usually decreased and there is a dyspnea with exertion. The psychological effect of the poor posture and the sunken chest is very important in both girls and boys. This is especially dis-

6. Dorner, R. A.; Keil, P. G., and Schissel, D. J.: Pectus Excavatum: Case Report with Pre- and Postoperative Angiocardiographic Studies, J. Thoracic Surg. **20**:444, 1950.

7. Ravitch, M. M.: Pectus Excavatum and Heart Failure, Surgery **30**:178, 1951.

tressing to young girls but may be of equal concern to the boy who has to bear the comments of his friends at the swimming pool. These persons are handicapped by the deformity to a greater extent than is evident to themselves or to their parents. Their situation is analogous to that of the child with the patent ductus arteriosus, where frequently the parents consider the child normal in all regards. They are amazed at the great improvement after operation, and not until then do they realize the subtle effects of the handicap.

Our patients have been divided into two groups: 6 infants who have had the limited operation and 12 children (over 2 years of age) who had the complete operative procedure. The infants were between the ages of 3 and 15 months, and all had symptoms referable to the deformity. All had an increasing deformity with marked retraction. All had stridor, and three had nearly constant respiratory infections, with one being a severe feeding problem with nausea and vomiting. Of the remaining 12 patients, 10 were between the ages of 2 and 7 years. One child was 10 years old and one was 16. The deformity was most marked in the older group and this was the main indication for operation. Five of these had stridor, and nearly all were underweight and less rugged than other children of comparable age.

OPERATIVE PROCEDURE

Intratracheal anesthesia was used in all patients. The "limited" operation has been used in infants who have symptoms and consists of a division of the soft-tissue attachments to the sternum.[2] In the narrow type of the deformity the substernal ligament is often thick, under tension, and when divided the cut ends will separate widely. This may be sufficient to overcome the marked retraction, but it is usually necessary to divide the shortened anterior portion of the central tendon of the diaphragm as well. In the broad type of the deformity the diaphragmatic attachments must be divided laterally to the nipple line before retraction ceases. These infants usually tolerate anesthesia poorly until the attachments are divided and their improvement is then dramatic. The procedure is simple, requires a short operating time, and is performed through a short transverse or longitudinal incision at the level of the xiphoid.

The complete operation is shown by the diagrams. A longitudinal midline incision is made from the level of the second rib to below the xiphoid, and the attachments of the pectoral muscles are reflected laterally to beyond the costochondral junctions. The rib cartilages are freed subperichondrally from the sternum laterally to the beginning of the deformity and divided (Fig. 3). The posterior attachments of the sternum are then divided (Fig. 4) to the upper border of the deformity between the second and third interspace. This allows the pleura and pericardium to drop posteriorly, and the heart shifts to the normal position. A transverse cuneiform osteotomy is then performed between the second and third interspaces and the sternum held in its corrected position by several heavy nonabsorbable surgical (silk) sutures (Fig. 5). It may be necessary to perform several osteotomies to mold the sternum to its normal contour. The excess cartilage is then resected, and the third and fourth cartilages are usually resutured (Fig. 6) with silk or stainless-steel wire. The lower cartilages are usually left free, and there has been no difficulty with paradoxical respiration. The most important feature is a wide resection of the attachments of the sternum, as far as the upper limit of the deformity.

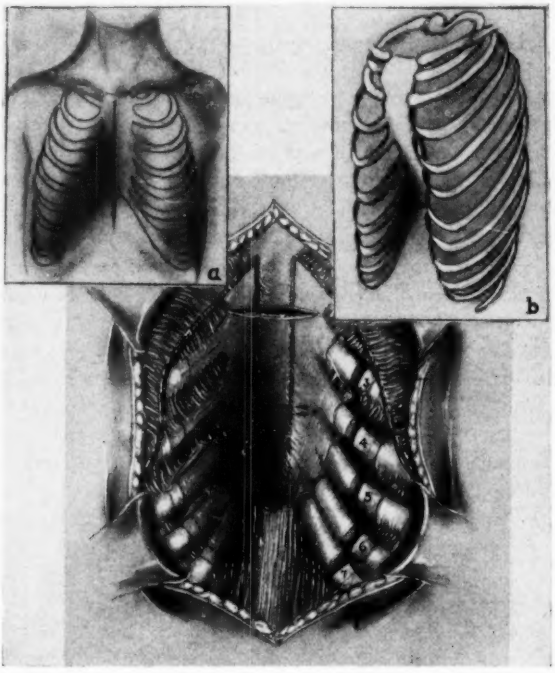

Fig. 3.—Pectoralis major is reflected laterally and the costal cartilages exposed. The cartilages have been divided on the left, and the site of the osteotomy is shown.

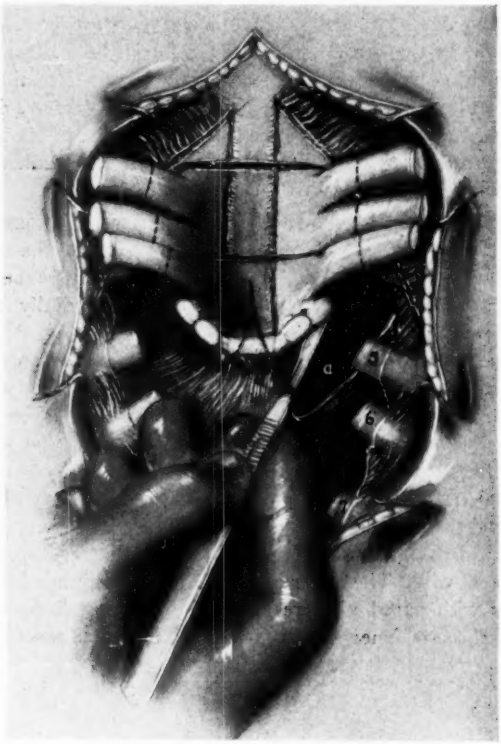

Fig. 4.—Attachments of the diaphragm are being divided, exposing the pleura and pericardium.

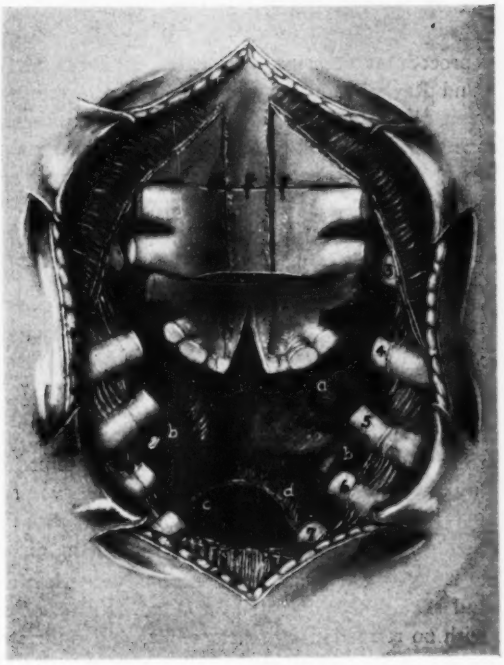

Fig. 5.—Sternum is free and three osteotomies are shown. (*a*) Pericardium; (*b*) pleura; (*c*) peritoneum; (*d*) diaphragm.

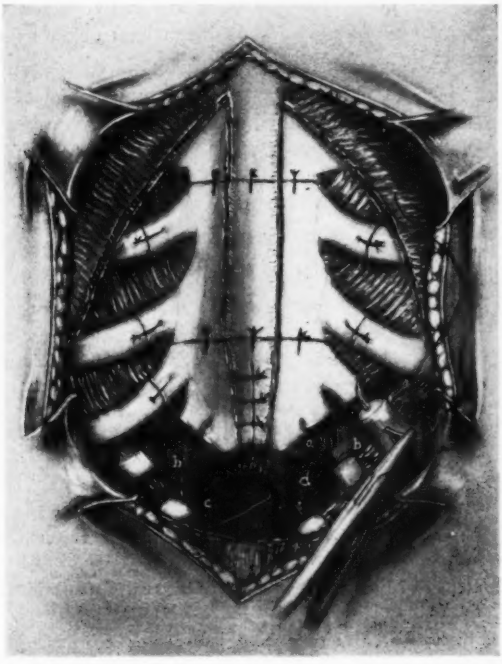

Fig. 6.—Completed procedure with the sternum in corrected position.

The operative procedures described by others do not differ greatly from our method. Lester [8] and Ravitch [9] do not resuture the costochondral junctions. We have resutured all the ribs in some cases, none of them in others, and now prefer the technique described. Lester [8b] and Lindskog [3] use external traction, but we have not found this necessary. The only reason for traction is stabilization of the chest, for if the sternum will not remain in its corrected position without traction the deformity will probably recur. We have not used the osteoperiosteal rib graft strut described by Dailey.[10] Miscall [11] has reported the use of a Kirschner wire to support the sternum which later penetrated the pericardium, and we have not used this procedure.

OPERATIVE RESULTS

Our patients have been followed one to five years. The first patient (Case 1) was operated on five years ago, with an excellent functional and structural result and no tendency to recurrence of the deformity. The limited operation has been used in six infants. All have had immediate relief of their symptoms. Two patients had only slight deformity after three years, but the other four have persistent deformity and should be reoperated on in the future. It is of interest that these patients now have minimal retraction with deep inspiration in spite of the deformity.

Twelve patients have had the complete operation. One has a 50% recurrence of the deformity and should be reoperated on. One patient has a good correction of the depression with no retraction, but a slight rotation of the sternum developed. The remaining 10 have what we consider an excellent result. The sternum is in normal position, there is no retraction, and their posture is improved. A more subtle but important result of the operation has been an improvement in the patient's general well-being. They are more active and tire less easily. Their exercise tolerance is improved, and they do not have dyspnea with ordinary exertion.

There have been no operative deaths, and the children tolerated the procedures very well. One child had a Staphylococcus aureus wound infection which drained intermittently for six months and has remained healed for two years. Four patients have had postoperative pneumothorax which required aspiration. One of these required the insertion of an intercostal catheter a few hours after operation, which was left in place for 24 hours.

REPORT OF CASES

The following case reports illustrate the problems which we have encountered.

CASE 1.—*No recurrence of the deformity after four and one-half years*

M. M., a 2½-year-old boy, was first seen in September, 1949, because of a "noisy" difficult breathing and a deformity of the anterior chest wall (Fig. 7). The deformity had been noted shortly after birth, and it had increased in severity. The child had frequent respiratory infections with respiratory stridor. Examination revealed an infant small for his age. There was marked

8. (*a*) Lester, C. W.: The Surgical Treatment of Funnel Chest, Ann. Surg. **123**:1003, 1946; (*b*) Funnel Chest and Allied Deformities of the Thoracic Cage, J. Thoracic Surg. **19**:507, 1950.

9. Ravitch, M. M.: The Operative Treatment of Pectus Excavatum, Ann. Surg. **129**:429, 1950.

10. Dailey, J. E.: Repair of Funnel Chest Using Substernal Osteoperiosteal Rib Graft Strut: Report of a Case with 4 Year Follow-Up, J. A. M. A. **150**:1203, 1952.

11. Miscall, L., in discussion on Dorner; Keil, and Schissel.[6]

depression of the lower end of the sternum at the junction of the gladiolus and xiphoid, with marked retraction on inspiration. Respirations appeared labored. The lungs were clear to percussion and ausculation. Laboratory findings were within normal limits.

Operation was performed on Sept. 9, 1948. The costal cartilages of the third, fourth, fifth, sixth, and seventh ribs were resected and cuneiform osteotomies were performed between the

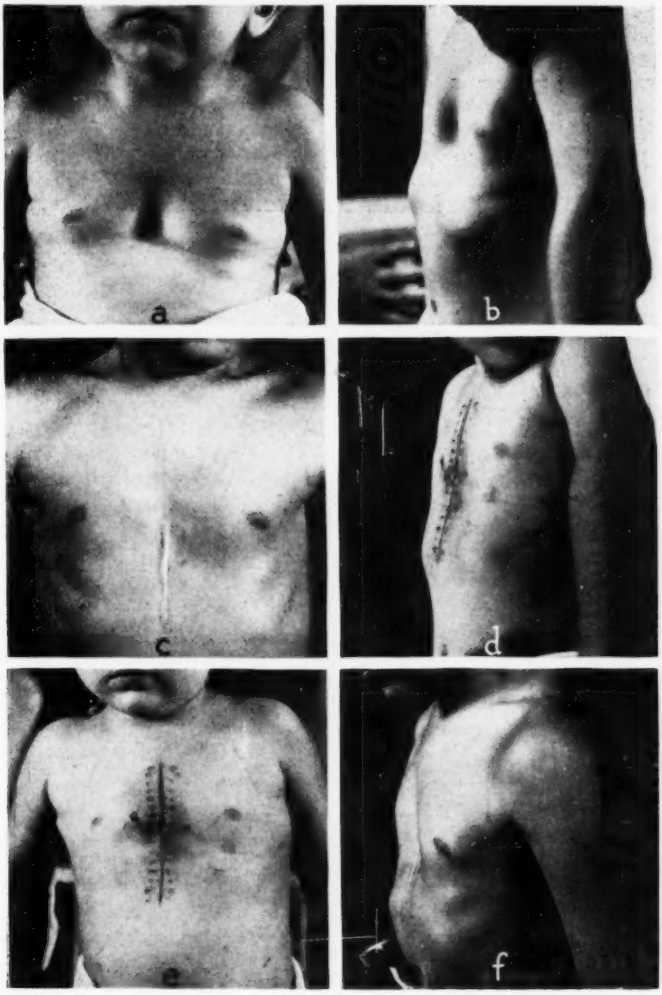

Fig. 7 (Case 1).—Preoperative deformity (*a* and *b*); immediate postoperative appearance (*c* and *d*); correction maintained four and one-half years after operation (*e* and *f*).

second and third ribs and between the fourth and fifth ribs. A stainless-steel wire was passed through the sternum, and the two ends were brought out on either side of the wound and fastened to a "Jacob's Ladder" for traction.

The convalescence was uneventful except for a small right pneumothorax which did not require aspiration. His general condition is now excellent. The sternum is stable and has main-

tained the corrected position. There is no retraction on inspiration. It is significant that there has been no recurrence of the deformity in spite of rapid growth during four and one-half years.

CASE 2.—*Infant who had severe respiratory and gastrointestinal symptoms as a result of the deformity who had striking relief after a limited operation and in whom the deformity is improved but not completely eradicated*

S. S., an 8-month-old boy, was first seen on Feb. 21, 1949, because of stridor and persistent vomiting. The infant had been a feeding problem since birth, requiring thickened feedings and administration of atropine. He had had repeated respiratory infections with "croup."

Examination revealed a poorly nourished boy 8 months old. There was a "broad" funnel-chest deformity with marked retraction. Respirations were very labored. The remainder of the examination revealed nothing significant. Routine laboratory studies showed no abnormalities. Because of the vomiting, a gastrointestinal series was done, which was negative. The nose and throat consultant could find no evidence of respiratory tract obstruction.

A "limited" operation was performed, dividing the attachments of the substernal ligament and diaphragm to the sternum. The substernal ligament was under marked tension and separated widely after division. The immediate improvement in respiration was dramatic, and the patient had no further vomiting after the operation.

Since operation the child has been healthy and has developed normally. There is still some deformity but it seems to be decreasing with growth. It is possible that he may not require further operative correction.

CASE 3.—*A severe deformity in a 5-year-old child with symptomatic relief after complete correction*

L. Y., a 5-year-old white girl, was admitted in October, 1952, because of a deformity of the anterior chest wall (Fig. 8). The deformity had been noted shortly after birth and had been progressive. The patient had dyspnea with mild exercise and frequent colds; she had had two bouts of pneumonia during the previous year with slow resolution. There was no family history of chest deformity.

Physical examination revealed that the patient was a fairly well-developed white girl of 5 years. The findings on general examination were negative except for the chest. There was a deep narrow funnel-chest deformity with marked retraction on inspiration. The heart was displaced to the left by percussion and by x-ray. Laboratory findings were within normal limits.

At operation on Oct. 31, 1952, the operative procedure was exactly as shown in the illustrations. No postoperative traction was used. The postoperative course was complicated by a temporary right pneumothorax which was treated by closed intercostal catheter suction for 24 hours. Thereafter her course was uneventful.

The sternum is now stable, and it has a normal contour. There is no retraction with inspiration. Her general condition is greatly improved. She has no dyspnea with exertion; she is more active and recovers more promptly from respiratory infections.

CASE 4.—*Correction of the deformity appearing adequate 10 months after operation but displacement of the sternum after two years*

R. B., was 7 years of age when seen in June, 1950. He had mild spastic paraplegia, and the chest deformity had been noted at birth. Stridor had been present frequently since birth, and the pediatric service believed the funnel-chest deformity was an important contributing factor. He had been under treatment for the spasticity for several years and was able to walk with a fairly normal gait. His mental status was good.

Examination revealed a well-developed boy aged 7 years. The positive physical findings were spasticity of the extremities and a rather broad funnel-chest deformity with deep retraction. The heart was not displaced. Laboratory findings were noncontributory.

At operation on Jan. 25, 1951, the usual complete procedure was used, resecting the costal cartilages of the third, fourth, fifth, sixth, and seventh ribs. There was marked tension on the anterior attachments of the diaphragm extending laterally to the nipple line. When these attachments were divided, the retraction ceased. The costal cartilages were resutured with silk.

The postoperative course was uneventful, and he has had less stridor. In April, 1951, the repair seemed in good condition and there was no retraction. The patient was reexamined in

February, 1952, and angulation of the sternum had developed. The sternum was rotated on its long axis so that the left side was anteriorly displaced and the right side was depressed posteriorly. A second operation is planned for repair.

CASE 5.—*A 9-month-old infant who had the limited operation because of minor symptoms in whom the deformity has progressed, requiring operative correction*

C. B., a 9-month-old infant, had a deformity of the anterior chest wall at birth, which had progressively increased. The infant had sterterous breathing associated with upper respiratory

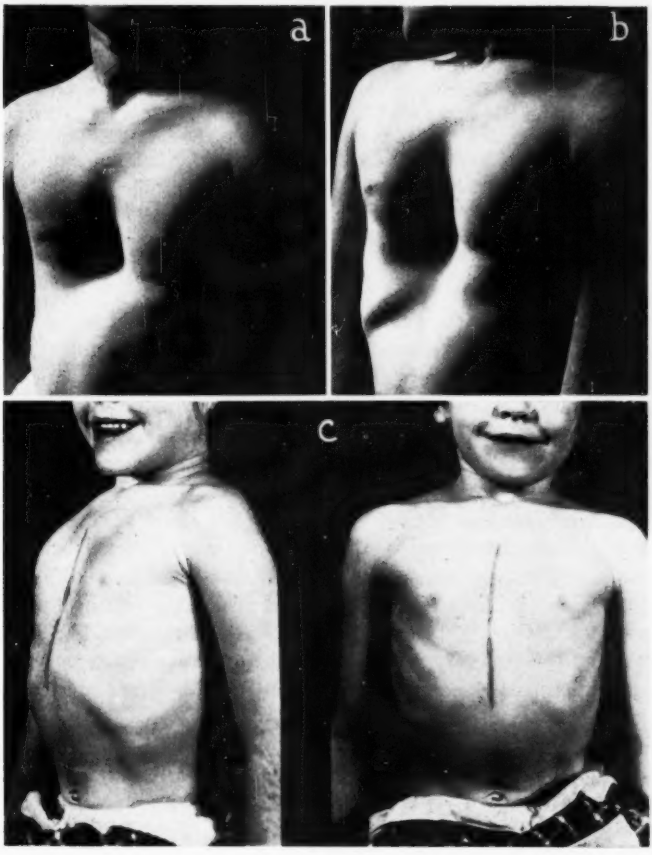

Fig. 8 (Case 3).—Preoperative deformity (*a* and *b*; note retraction with inspiration *b*); postoperative correction with no retraction (*c*).

infections but no other symptoms, and his growth had been normal. There was no family history of chest deformity.

Physical examination revealed that the infant appeared healthy and well nourished. The only positive physical findings were related to the chest. There was a marked depression of the lower end of the body of the sternum and marked retraction with inspiration. Fluoroscopy showed the heart displaced to the left, and there was very limited motion of the anterior portion of the diaphragm.

Operation was performed on Sept. 16, 1950. The limited procedure was done with division of the substernal ligament and the anterior attachments of the diaphragm. The postoperative con-

valescence was uneventful, and for a few months the deformity appeared to improve. The condition has since progressed, and at present there is marked depression and retraction.

CASE 6.—*A 10-year-old boy with a funnel chest and rotational deformity of the sternum*

N. F., a 10-year-old boy, was admitted on June 27, 1952. He was known to have had increasing deformity of the sternum since infancy. His parents noticed that the child tired more easily than others.

A marked funnel-chest deformity was found on physical examination. The sternum was depressed and rotated through almost 90 degrees on its long axis. X-rays showed typical funnel-chest deformity, with the heart displaced into the left chest. The xiphoid nearly touched the spine.

An extensive operative procedure was done with wedging of the left costal cartilages from the second through the costal margin. The right costal cartilages were all resected from the second to the margin of the deformity. These were shortened 3 or 4 cm. After a transverse osteotomy through the second interspace in the body of the sternum, the depression and rotational deformity could easily be corrected. The costal cartilages were repaired with silk sutures to the perichondrium.

Five months after the procedure there was a good correction of the deformity and partial return of the cardiac shadow to the midline. The child is more active and tires less easily.

CONCLUSIONS

At present we feel that the limited operations of Brown should be used only in infants with severe deformity and retraction who are having symptoms. The symptomatic improvement is frequently dramatic, but most of these children will require a secondary operation. If the children are not having symptoms but do have a progressive deformity we prefer to delay the operation until they are about 5 years of age. This now seems the ideal time for correction because (*a*) the full extent of the deformity is evident; (*b*) the secondary effects such as kyphosis have not become permanently established; (c) the cartilaginous structures are still pliable and can be readily manipulated, and (*d*) the deformity is corrected before the child enters school. (We have seen several children who at 2 years of age had what appeared to be a definite deformity, but spontaneous improvement followed and they appeared normal at 4 years.) The operation is well tolerated by young children and the results now seem very satisfactory. The operative repair in older children and young adults can be done satisfactorily, but there may be persistent secondary deformities.

DISCUSSION

DR. PAUL F. HAUSMANN, Milwaukee: My colleagues and I recently reviewed the results of our operations in 50 cases at Milwaukee Children's Hospital, Milwaukee Passavant Hospital, and several other hospitals at which we practice and have come to somewhat the same conclusions as Dr. Mahoney, except that it took us a little longer to do so.

[Slide] We have 50 consecutive cases in our service. You can see the ages of the patients—only four were under 6 months. The bulk of our series lies in the age groups between 6 months and 2 years. Our experience was the same as the others. The great majority of patients were male.

[Slide] We were able to accomplish a simple operation in only two infants. In the others we felt that the deformity was too large to warrant just the simple procedure. We have done the extensive operation in 48 cases and have had to do no other operations or reoperations.

Regarding the substernal ligament, we have found this structure hypertrophied in only 13 cases; it was normal in 37.

We have had no deaths. We encountered one infected wound, which occurred in one of the patients in the older age groups.

We have not determined what the etiologic agent might be. We do not believe that the ligament is the etiologic factor. Hereditary incidence was present in half of these patients.

As far as we are concerned, the primary problem is as follows: When is the ideal time to do the operation? We believe that only observation of a large series of cases, both operative and nonoperative, will furnish the answer to this problem. We feel that the small operation has no application in any other than the very young infant. It cannot be done in the presence of any upper respiratory obstruction, or the deformity will promptly recur.

After the age of 2 or 3 months, we feel that in almost all cases the larger procedure is necessary. This can be delayed until the child is from 12 to 18 months old, since the deformity does not progress greatly, usually, and the child is a better surgical risk. In some patients the deformity actually regresses, and a very few can be spared surgery if they are watched until they are a year old.

We feel that the ideal age for surgery—the group in which the best results can be achieved—is the group between 12 and 24 months of age, although the results, on the whole, were satisfactory through the age of 6 years.

We feel that subperichondral resection should be done. Actually, with regeneration of the cartilages, stability of the chest can be obtained in 12 to 14 days. After the age of six years, cosmetic results are not as good because the normal contour of the chest is altered. It is flattened in the anterior-posterior projection. The chest is broadened transversely. There are transverse furrows, and these cannot be completely corrected.

SURGICAL ASPECTS OF SPONTANEOUS HYPOGLYCEMIA DUE TO OCCULT INSULINOMA

F. A. dePEYSTER, M.D.
AND
R. K. GILCHRIST, M.D.
CHICAGO

A DIAGNOSIS of an insulin-secreting tumor is tenable when the clinical symptom-complex conforms with the criteria set forth in Whipple's triad. These criteria are as follows: (1) signs and symptoms of insulin shock usually progressive, frequently induced by fasting or exercise; (2) repeated fasting blood-sugar concentrations below 50 mg. per 100 cc., and (3) symptomatic relief by dextrose administration.

More than 400 cases of hypoglycemia due to pancreatic adenoma are reported in the literature, in half of which surgical treatment was employed. In about 45% of the patients explored, no tumor could be located by the surgeon. In more than one-half of these cases in which the surgeon did not find the tumor but proceeded with a subtotal pancreatectomy, the resected specimen was histologically normal. The over-all cure rate in patients is about 40% when the surgeon, in spite of finding no tumor, performs a subtotal pancreatic resection.[1]

Reported cases[2] of occult insulin-secreting adenomas in which the lesion was not detected at surgery but was cured by an initial pancreatic resection are listed in the accompanying Table.

Three cases of occult pancreatic insulinoma are presented which, it is hoped, may contribute toward improving the cure rate and to solving the dilemma faced by the surgeon, who, after careful exploration, fails to find the offending pathology.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 6, 1953.

The term "insulinoma" used throughout the paper denotes an insulin-secreting islet cell adenoma of the pancreas.

From the Department of Surgery, Presbyterian Hospital, affiliated with the University of Illinois College of Medicine.

1. Howard, J. M.; Moss, N. H., and Rhoads, J. E.: Collective Review: Hyperinsulinism and Islet Cell Tumors of the Pancreas, Internat. Abstr. Surg. **90**:417-455 (May) 1950.

2. (*a*) Footnote deleted. (*b*) Smith, J.: Hyperinsulinism, Wisconsin M. J. **38**:283-286 (April) 1939. (*c*) Priestly, J. T.; Comfort, M. W., and Radcliffe, J., Jr.: Total Pancreatectomy for Hyperinsulinism Due to Islet Cell Adenoma: Survival and Cure at 16 Months After Operation: Presentation of Metabolic Studies, Ann. Surg. **119**:211-221 (Feb.) 1944. (*d*) Frantz, V. K.: Adenomatosis of Islet Cells with Hyperinsulinism, Ann. Surg. **119**:824-844 (June) 1944. (*e*) Lopez-Kruger, R., and Dockerty, M. B.: Tumors of the Islets of Langerhans, Surg., Gynec. & Obst. **85**:495-511 (Oct.) 1947. (*f*) Brown, G. M.: The Effect of ACTH on a Case of Islet Cell Adenoma of the Pancreas, Am. J. Digest. Dis. **18**:145-146, (May) 1951.

Cases of Occult Insulin-Secreting Adenomas Not Detected at Surgery but Cured by an Initial Pancreatic Resection

Authors	Age, Yr.	Sex	Chief Symptoms	Duration	Fasting Blood Sugar, Mg. per 100 Cc.	Operation	Pathology	Location	Size	Result
Engle and Orr.....	55	F	.....	.....	..	Subtotal pancreatectomy	Adenoma	.....	.....	Cured
	38	F	.....	.....	..	Subtotal pancreatectomy	Adenoma	.....	.....	Cured
Smith [2b] and Brown in discussion on Engle and Orr.....	35	F	Weakness, sweatiness, dizziness, semicoma	9 yr.	25	Subtotal pancreatectomy, 22 gm. removed	Adenoma (suspiciously malignant)	.....	.....	Cured
Priestly; Comfort, and Radcliffe [2c]....	49	F	Sweating, dizziness, confusion, unconsciousness (1-5 hr.)	3 yr.	30	Total pancreatectomy	Adenoma	Head	8 × 5 × 5 mm.	Cured but a controlled diabetic
Frantz [2d] (Case 30).....	46	F	Fainting spells in a. m.; twitching, headaches	2-6 mo.	37	Subtotal pancreatectomy	Adenoma and calcified multiple adenoma	Tail	5 mm.	Cured 6 mo. postoperatively
Lopez-Kruger and Dockerty [2e].....	..	..	.....	.....	..	Resection tail and body	Adenoma	.....	2 × 5 mm.	Cured
	..	..	.....	.....	..	"Resected suspicious tissue" reported negative by pathologist; subsequent review of specimens revealed tumors	Adenoma	.....	4 mm.	Cured
Brown [2f]	60	F	Confusion, restlessness, transient hemiplegia	6 mo.	39	Subtotal resection	Adenoma	Tail	12 mm.	Cured
dePeyster and Gilchrist.....	46	M	Diplopia, weakness, tremor, coma	6 mo.	26	Subtotal pancreatectomy, splenectomy	Adenoma	Tail	12 × 15 mm. 11 × 7 × 4 cm.	Cured
	47	F	Weakness, excitability, confusion, convulsions	8 yr.	16-18	Subtotal pancreatectomy (70 gm.), splenectomy, cholecystectomy	Adenoma	Junction body and head (15 cm. from tail)	2 × 2 × 1 cm.	Cured

REPORT OF CASES

CASE 1 (Referred by Dr. R. T. Woodyatt).—B. L., a 47-year-old white housewife, was admitted to the hospital on March 30, 1944, because of daily episodes of convulsions terminating in coma (present for two years).

Ten years prior to admission the patient experienced frontal headaches, associated with profuse sweating. These symptoms became more intense and were associated with increasing drowsiness, crying spells, irrationality, and convulsions terminating in coma. Orange juice or milk taken about 5 a. m. would prevent the symptomatic distress. The intravenous administration of dextrose would relieve the symptoms. Fasting blood-sugar determinations on previous occasions ranged from 30 to 40 mg. per 100 cc. She had previously received radiation therapy (3,000 r) over the hypophysis without symptomatic benefit. (There was x-ray evidence of thinning of the posterior clinoids suggesting erosion [questionable] tumor.)

Physical Examination.—Examination revealed an obese, rational, and cooperative woman, 5 ft. (152 cm.) tall and weighing 185 lb. (84 kg.). The general physical examination revealed nothing abnormal.

Laboratory Data.—Repeated fasting blood-sugar determinations ranged from 30 to 40 mg. per 100 cc. Values for the glucose tolerance test were 80, 110, 120, 130, 110, 80, 60, 60, and 50 mg. per 100 cc. Other blood chemistries were normal. The Hanger test was negative. The basal metabolic rate was + 5 to — 15%. There was x-ray evidence of thinning of the posterior clinoids, suggesting erosion.

First Operation (Dr. V. C. David).—On May 26, 1944, through a transverse upper abdominal incision the pancreas was explored after complete duodenal mobilization. No tumor was detected. Subtotal pancreatectomy was performed, removing all of the gland to the left of the superior mesenteric vessel including the spleen. Pathological examination revealed no abnormality of islet tissue or evidence of adenoma. Shortly after surgery, convulsions with coma recurred. Pneumonia developed which responded satisfactorily to chemotherapy.

Alloxan was administered intravenously in doses of 150 and 250 mg. per kilogram, each for three days respectively. There was no apparent beneficial effect. No significant toxic signs or symptoms were noted.

Second Operation (Dr. V. C. David).—On July 21, 1945, the remaining pancreas to the right of the superior mesenteric vessel and portal vein was removed except for a 3 gm. remnant adjacent to the pancreatic duct where it entered the duodenum. The patient's clinical course was not benefited by the surgery. Pneumonia again developed which responded to chemotherapy. Hypoglycemic convulsions could be prevented by frequent feedings. The patient remained hospitalized as a "boarder."

Third Operation (Dr. R. K. Gilchrist).—On Dec. 3, 1947, a total pancreatectomy and duodenectomy was performed, since no tumor was detected at surgery in the small remnant of the pancreas. Examination of the surgical specimen disclosed an islet cell tumor buried deep in the head, lying near the duodenum. The diagnosis was confirmed by frozen section histology. One and one-half hours following surgery, hyperglycemia with a 2% glycosuria was observed. For the third time pneumonia developed postoperatively. The patient did not recover from this illness.

Pathology Report (Dr. G. M. Hass).—The specimen consisted of the head of the pancreas and adjacent duodenum (Fig. 1). The maximum dimension of the pancreas in the antero-posterior axis was 20 mm. and in the superior-inferior axis, 45 mm. Near the superior margin and at a distance of approximately 12 mm. from the wall of the duodenum there was a tumor which measured 25 by 15 by 20 mm. in its maximum dimensions. It was roughly ellipsoidal in shape. The cut surface disclosed slight lobulations, but these were not very distinct. About two-thirds of the tumor was dark red. This appeared to be due to hemorrhage and congestion rather than to necrosis.

Histology.—Two sections through the specimen revealed a tumor which was fairly well circumscribed (Fig. 2). It was surrounded by fibrous tissue and compressed pancreatic tissue. The tumor was very rich in blood vessels. It consisted of cords of small cells having

a vesicular nucleus and a slightly vacuolated cytoplasm. There was a tendency for these cells to form alveoli. No specific granules could be made out within the cytoplasm of the cells. The tumor was an adenoma of the islet cells. It was impossible to say, however, of which cell.

Diagnosis.—The diagnosis was adenoma of insular tissue.

CASE 2 (Referred by Dr. L. Avery).—M. R., a 57-year-old white housewife, entered Presbyterian Hospital on April 4, 1951, because of daily convulsions.

Fig. 1 (Case 1).—Surgical specimen cut transversely, showing dark-red adenoma in remnant of pancreas adjacent to sectioned duodenum (marked *X*).

The patient had been well until eight years prior to admission when she began to experience undue excitement and agitation followed by episodes of tearing at her clothes and "acting queerly." These episodes occurred in the morning and were precipitated by strain. They became progressively frequent and more intense, rendering the patient unconscious for unknown periods. Because the attacks began to occur daily and terminate in coma, the patient sought medical care.

Hospital Course.—The patient was given Mesantoin (3-methyl-5, 5-phenylethyl hydantoin) white woman appearing healthy. General and special examinations were within normal limits.

Laboratory Data.—The blood-sugar level during hypoglycemic attacks ranged from 18 to 45 mg. per 100 cc. The values for the glucose tolerance test curve were 30, 40, 40, 40, 30, and 30 mg. per 100 cc. Other blood chemistries were normal. X-rays of the skull revealed nothing abnormal. The electroencephalogram was interpreted as showing distortion of alpha activity and bursts of abnormal slow activity throughout periods. There was a big build-up during ventilation, which was most prominent in the parietal channels. The corticotropin stimulation test revealed 47% drop in the eosinophile count at four hours.

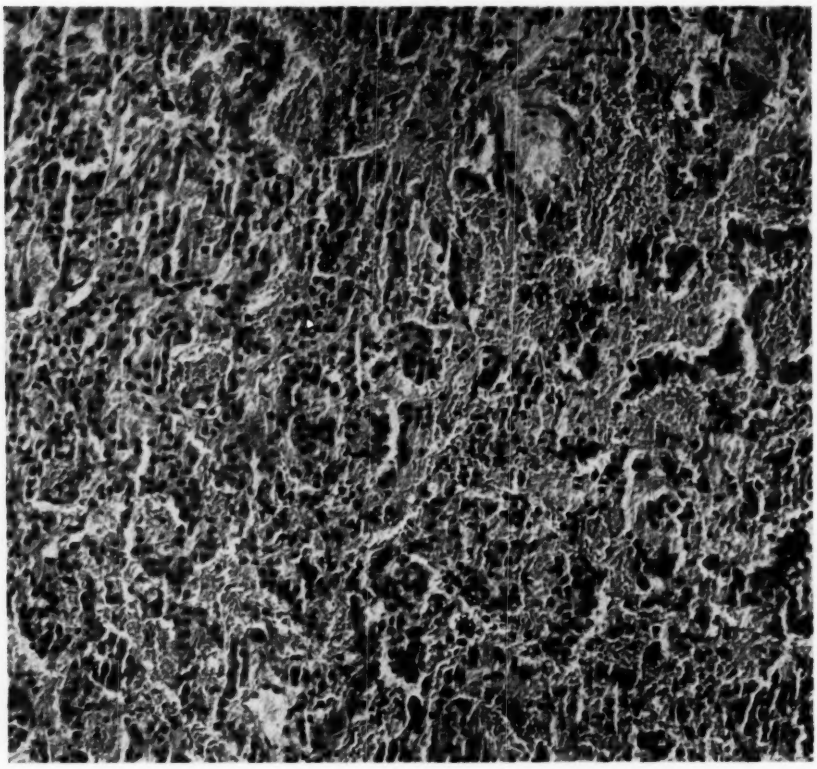

Fig. 2 (Case 1).—Photomicrograph of insulin-secreting adenoma, showing cords of tumor cells dispersed in a stroma rich in blood vessels. Crystalline violet; × 200.

Hospital Course.—The patient was given Mesantoin (3-methyl-5, 5-phenylethyl hydantoin) and dietary management, with 200 cc. of milk three times a day as in-between feedings. Frequent seizures occurred ending in unconsciousness. Immediate symptomatic relief was obtained by intravenous administration of 50% dextrose. Seizures could be aborted by the ingestion of sugar cubes. Corticotropin, 50 mg. or more per day, would prevent hypoglycemic attacks. However, cortisone (Cortone), up to 50 mg. per day proved ineffective, probably because of an inadequate dose employed.

Operation (Dr. R. K. Gilchrist): On June 11, 1951, through a transverse incision the abdomen was opened, the duodenum mobilized, and the pancreas explored without evidence of tumor. A subtotal pancreatectomy was carried out, leaving about a 1 cc. remnant of the

head to the right of the portal vein. The spleen was also removed. Cholecystectomy was performed, extirpating a chronic thickened gall bladder with stones. Penrose drains were placed to the pancreatic stump and the abdominal wall closed. During closure, serial section of the pancreas revealed a 4 mm. adenoma located 3 mm. from the transected pancreatic edge. The blood-sugar level increased from 85 mg. per 100 cc. before celiotomy to 250 mg. per 100 cc. within four hours following resection of the pancreas containing the adenoma. Hyperglycemia persisted nine days before the blood sugar returned to normal fasting levels of 110 to 115 mg. per 100 cc.

Postoperative Course: The patient made an uneventful recovery and was discharged as cured on the 18th postoperative day.

Follow-Up.—The patient has been in excellent health since operation. Physical examination on Feb. 7, 1953, revealed nothing abnormal. The fasting blood sugar was 108 mg. per 100 cc. The glucose tolerance curve was interpreted as being normal.

Pathology Report (Dr. G. M. Hass).—In the body of the pancreas near the head, at a distance of 18 cm. from the tip of the tail of the pancreas there was a tumor nodule measuring

Fig. 3 (Case 2).—Transected surgical specimen of pancreas showing occult adenoma revealed only by serial section after subtotal pancreatectomy.

2 by 2 by 1 cm. (Fig. 3). It could not be seen from either the anterior or posterior surface of the pancreas until after it was cut. The cut surface revealed a lesion of the same consistency as the surrounding pancreas, and it was impossible to tell its limits by palpation. The tumor was sharply circumscribed with a capsule. It was slightly pinker than the rest of the pancreas and was homogenous and moderately translucent. The remainder of the pancreas was examined by multiple transverse sections, and no other tumor nodules were identified.

Histology.—The tumor, which was fairly well circumscribed with a poor capsule, was composed of cells which closely resembled those seen in the more normal islands of Langerhans (Fig. 4). They had grown in long cords between which there were many sinusoids engorged with blood. Very rarely could mitotic figures be seen; however, the general architectural pattern was that of a benign lesion.

Diagnosis.—The diagnosis was adenoma of insular tissue with hyperinsulinism.

Case 3.—J. C., a 63-year-old white man, a dairy farmer, was admitted because of periods of tenseness, weakness, dizziness, and coma, present for two months.

The patient was well until about six months prior to admission, at which time, while he was working in the corn field, diplopia developed, followed by weakness and nervousness. Two months before admission he became weak and nervous before breakfast with recurrent diplopia followed by coma. The patient recovered when aroused and was given food. Similar attacks were experienced which became progressively severer, occurring principally in the morning or when the patient missed a meal. For 10 days prior to admission he had similar attacks each morning.

Physical Examination.—Examination revealed a rather obese man. The general physical and neurological examinations were within normal limits.

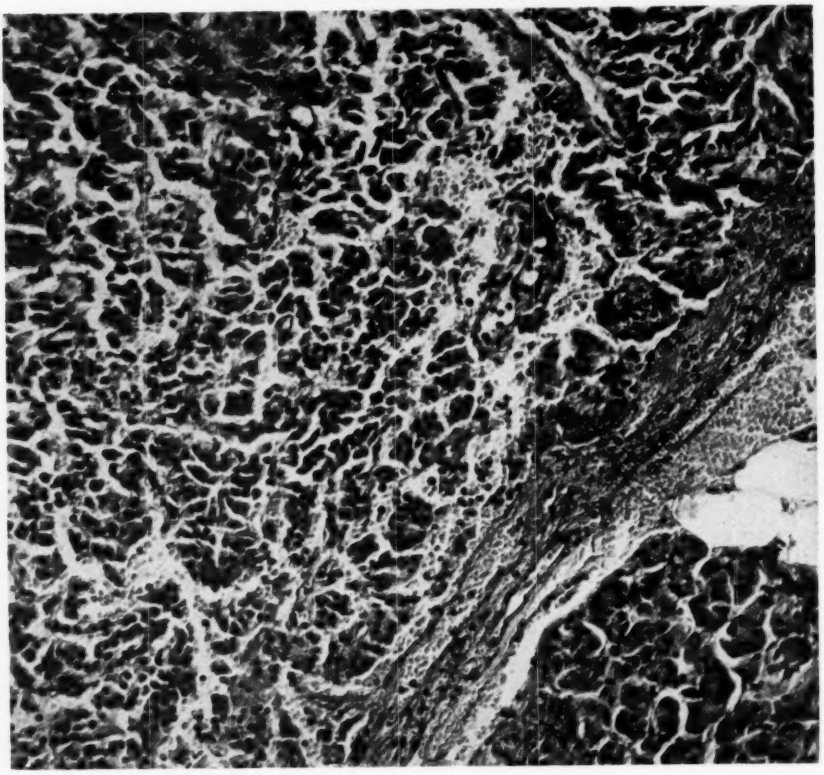

Fig. 4 (Case 2).—Photomicrograph of insulin-secreting adenoma, showing encapsulated tumor with islet cells arranged in rosette pattern. Normal pancreas appears in lower right field. Hematoxylin and eosin; × 200.

Laboratory Data.—Fasting blood sugar was 26 mg. per 100 cc. The values for the glucose tolerance test were 33, 152, 200, 142, and 17 mg. per 100 cc. Other blood chemistries were normal. Skull x-rays revealed no abnormalities. The basal metabolic rate was —1% and 0.

Hospital Course.—The patient experienced attacks similar to those prior to admission which were relieved immediately by intravenous administration of 50% dextrose.

Operation (Dr. R. K. Gilchrist): On March 27, 1946, the abdomen was opened through a curved incision extending from one costal margin to the other. The pancreas was bared from one end to the other as far as possible after mobilization of the duodenum. It was impossible to feel any nodules in the pancreas. The tail of the pancreas reached just above the left kidney. It was intimately connected with the kidney, and it was very hard to feel

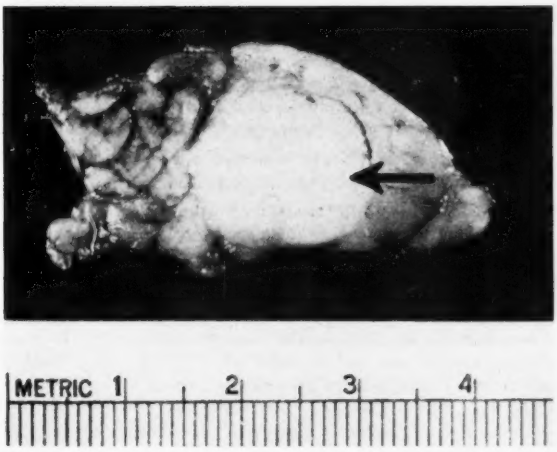

Fig. 5 (Case 3).—Surgical specimen of resected tail of pancreas, showing occult tumor revealed only by serial transverse sections, after subtotal pancreatectomy.

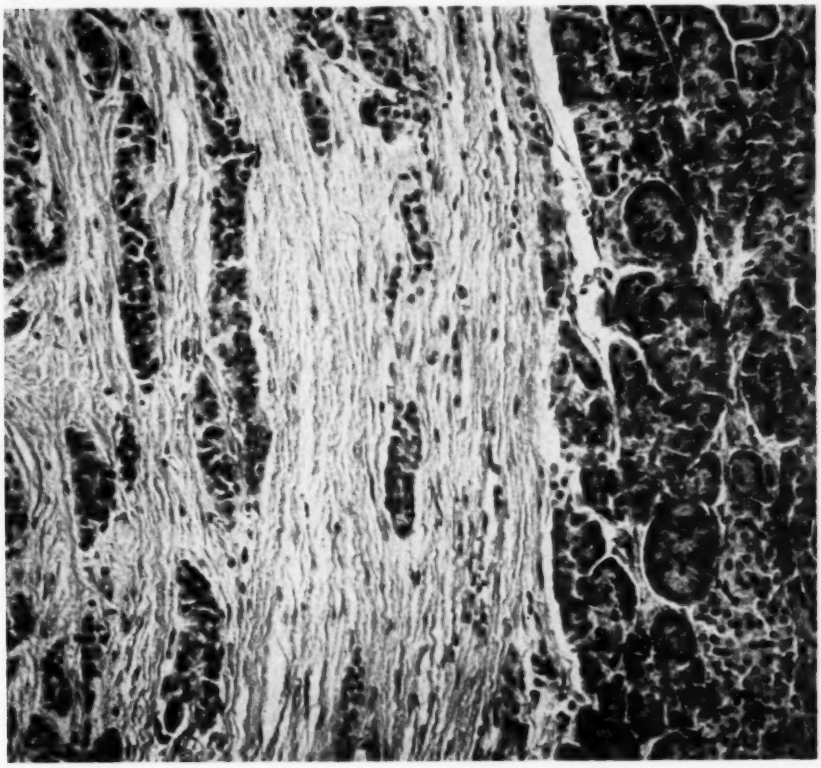

Fig. 6 (Case 3).—Photomicrograph of insulin-secreting adenoma, showing islet cells (predominately beta type) arranged in cords with some alveolar formation. Note dense stroma with comparatively few blood vessels, causing a white appearance of the gross tumor. Normal pancreas appears at right. Hematoxylin and eosin; × 300.

anything in this region with any certainty. The pancreas from one finger's breadth to the right of the superior mesenteric vessels was then resected, including the spleen. Two collapsible Penrose drains were placed to the stump of the sectioned pancreas. The surgical specimen was then sent to the pathology laboratory for immediate examination.

Blood-sugar determinations after surgery revealed a rise of more than 200 mg. per 100 cc. above a blood-sugar level determined prior to surgery.

Postoperative Course: There was a moderate amount of serosanguineous drainage fluid of a nonproteolytic type, originating in the wound, which ceased after 72 hours. An aspiration pneumonia developed which subsided with antibiotic therapy. The patient was discharged as cured on the 35th postoperative day.

Follow-Up.—When last heard from, Feb. 1, 1953, this patient was in good health.

Pathology Report (Dr. G. M. Hass).—The pancreas came to the laboratory in two parts (Fig. 5). One part weighed 60 gm. and the other about 10 gm. Apparently almost the entire pancreas had been removed with a large part of the splenic artery. Serial transverse cross sections were made through the pancreas. This disclosed a well-circumscribed, pale, white tumor with a circular outline. The tumor was partly embedded in the pancreas, but along one margin there was pancreatic fat tissue. The tumor measured about 12 to 15 mm. in its maximum dimensions. Serial sections through the tail of the pancreas showed no other tumors.

Histology.—The sections through the tumor, which included adjacent normal pancreatic tissue, afforded good opportunity to compare the types of cells in the tumor with those in the cells of the islets of the pancreas (Fig. 6). The tumor had a greater percentage of beta cells than did the adjacent islets of the pancreas. There was a considerable amount of stroma between the various masses and cords of cells, but there was no intermingling of normal pancreatic tissue with the tissue of the tumor itself. The tumor was essentially benign, and no recurrence or metastases should be expected.

Diagnosis.—The diagnosis was adenoma of insular tissue with hyperinsulinism.

COMMENT

Surgical excision of islet cell adenomas is the treatment of choice because 5 to 10% of the pancreatic adenomas are found to be malignant. Furthermore, irreversible damage to the central nervous system may result from progressive attacks of hypoglycemia, and, finally, an insulinoma untreated must be regarded as a potential fatal disease.

A temporary favorable response to adequate doses of corticotropin (Case 2) and cortisone may be expected.[3] This hormone therapy should be reserved for preoperative medical management, for patients refusing surgery, and for patients in whom the operative risk is considered too hazardous for survival. In certain instances patients may be encountered who are refractory to corticotropin even in doses up to 450 mg. per day.[4] This fact, in addition to the possible occurrence of undesirable side-effects resulting from prolonged corticotropin therapy, provides the chief limiting factor for the use of this hormonal management.

These three cases present several significant features. In each, Whipple's triad was observed, owing to the presence of an occult insulin-secreting adenoma; in each, the offending tumor was not detected on surgical exploration but discovered by the

3. Brown, H.; Hargreaves, H. P., and Tyler, F. H.: Islet-Cell Adenoma of the Pancreas: Metabolic Studies on a Patient Treated with Corticotropin and Cortisone, A. M. A. Arch. Int. Med. **89**:951-960 (June) 1952.

4. Kark, R., in discussion on McQuaire, I.; Ziegler, M. R.; Wright, W. S.; Bauer, E. G., and Ulstrom, R. A.: Further Studies of the Effects of ACTH on Spontaneous Hypoglycemiosis, Proceedings of the Second Clinical ACTH Conference, Philadelphia, Blakiston Company, 1951, Vol. 2, Ch. 5, pp. 69-80.

pathologist on serial section of the specimen and confirmed by immediate frozen section microscopy. An elevated blood-sugar level attended the extirpation of the offending tumor in all three patients.

The hyperglycemic rebound phenomenon has been previously described by McMillan.[5] He observed a blood-sugar level of 131 mg. per 100 cc. rise to 258 mg. per 100 cc. within 30 minutes following excision of a solitary insulin-secreting adenoma removed from the head of the pancreas. We observed a blood-sugar elevation with an accompanying glycosuria within one and one-half to four hours following subtotal pancreatectomy in which the occult adenoma was found within the surgical specimen. Undoubtedly the response took place more rapidly than our observations indicate.

SUMMARY AND CONCLUSIONS

In patients demonstrating Whipple's triad in whom no tumor is found on surgical exploration it would appear that subtotal pancreatectomy (at least to the right of the superior mesenteric vessels) should be performed. This operation

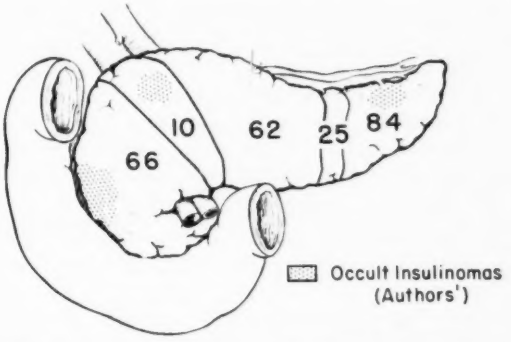

Fig. 7.—Distribution of pancreatic adenomas, modified from Howard.[1] Location of our cases of occult tumor are shown.

should yield a 75% chance of cure for occult adenomas, based on the distributional incidence of pancreatic insulinomas (Fig. 7).

Furthermore, subtotal pancreatectomy, according to David,[6] should provide a 50% chance of cure for hypoglycemia due to pancreatic hyperplasia and should benefit two-thirds of the patients with hypoglycemia in whom the resected pancreas is normal.

The adequacy of surgical therapy should be substantiated at the operating table while the abdomen is open by (1) the demonstration of an islet cell adenoma in the surgical specimen confirmed by rapid histological examination, and by (2) observation of a rise in the blood-sugar level following resection, as compared with the base level obtained from blood drawn during the exploration of the abdomen before the tumor is resected.

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5. McMillan, F. L., and Scheibe, J. R.: Islet Cell Tumor of the Pancreas, Am. J. Surg. **82**:759-761 (Dec.) 1951.

6. David, V. C., and Campbell, L. K.: Experiences in Subtotal Resection of the Pancreas in Hypoglycemia, Ann. Surg. **123**:836-846 (May) 1946.

A comparative hyperglycemic response in the presence of an islet cell tumor demonstrated in the surgical specimen would suggest adequate resection. However, if no significant rise in blood sugar is observed, despite a confirmed islet cell tumor in the operative specimen, further resection should be contemplated. Total resection of the pancreas harboring the occult tumor may be required before a significant rise in blood sugar is observed.

The utilization of these principles should substantially reduce the need for reoperation occasionally arising when multiple occult incretory tumors are present or when the insulinoma lies inaccessibly buried in the pancreatic head or in an ectopic site.

DISCUSSION

Dr. R. K. Gilchrist, Chicago: I could not feel these tumors either in the body or in the specimens, nor could the pathologist. These particular lesions were demonstrated by slicing the specimens into thin strips with a razor blade; thus, we seem to have had an unusual experience.

Dr. Brock Edwin Brush, Detroit: These cases reported by Drs. dePeyster and Gilchrist certainly are very interesting. It is true that these tumors may be extremely difficult to find grossly and sometimes even microscopically. As Dr. Frantz has shown, the pathologist must have a special interest in these tumors and study the resected pancreas very carefully if all the tumors are to be found. It should be remembered that multiple insulinomas have been found in 15% of cases and that in about 30 cases an occult insulinoma has been missed at the first operation, according to a recent review by Howard, Moss, and Rhoads.

When Dr. R. D. McClure and I presented our series of islet cell adenomas before this group in 1949, we included two cases in which no tumor could be found, and subtotal pancreatectomy gave an excellent result. We have since had two additional similar cases. In all four of these, hypertrophy and hyperplasia of the islet cells were found on microscopic study of the specimen, and in each there was a return of laboratory studies to normal with no subsequent return of symptoms in any case. However, when Dr. Whipple's criteria for diagnosis is present, a distinct tumor will be found in a very high percentage of cases.

METHOD OF GASTROINTESTINAL ANASTOMOSIS

EDWIN P. VARY, M.D.
FLINT, MICH.

THE VARIOUS methods of gastrointestinal suturing have probably received more attention through the years than any other subject in the technique of suture. This is evidenced by the great numbers of authors involved and the space and the illustrations devoted to the subject in the literature.

The origin of many types of suturing are lost in antiquity, and just when such patterns as the "cobbler's," the "furrier's," the "baseball" and "basting," and the "blanket or lock" stitch were adapted to gastrointestinal use we have been unable to determine. Many of the basic methods of suturing are still known by the names of the men who introduced them. Antoine Lembert [1] presented his inverting, interrupted, seromuscular stitch in 1826. Dupuytren advocated a continuous Lembert, and Halsted popularized his mattress variation. Czerny [2] contributed his interrupted suture before 1880 and advocated two layers. In 1886 Cushing [3] described a right angle continuous seromuscular suture which bears his name. This is the same as the continuous Lembert except that the bites are taken parallel to the wound instead of across it. Maunsell [4] described a through and through interrupted, single stitch, with the knots placed inside the lumen. He accomplished this by ingeniously intussuscepting the edges to be sutured through a window a few centimeters from the site of anastomosis. In 1890 Gregory Connell [5] described a through and through interrupted inverting suture placed from the outside on the anterior layer but with the knots inside. The untied ends of the last stitch were cleverly pushed through an interval on the opposite side. After the knot was tied and the ends cut the knot would then slip intralumenally. By 1903 he advocated making the method a continuous one, and it remains today the most popular through and through stitch for handling the forever troublesome anterior portion of the inner or primary layer. The forerunners of the Murphy button and its subsequent variations are further evidence that the anastomotic problem has been difficult.

Although recently the advances in the adjuncts of surgery, such as blood transfusion, vitamin therapy, nasogastric suction, electrolyte balance, and antibiotics, have

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 6, 1953.

1. Lembert, A.: Repert. gén. d'anat. et physiol. path., pp. 100-107, 1826.
2. Czerny, V.: Berl. klin. Wchnschr. **17**:641-642, 1880.
3. Cushing, H.: Tr. Am. S. A. **17**:297-305, 1899.
4. Maunsell, H. W.: Am. J. M. Sc. **103**:245-257, 1892.
5. Connell, F. G.: Surg. Gynec. & Obst. **4**:534-536, 1907; Am. J. Med. **5**:135-142, 1903; cited by Moynihan, B.: Abdominal Operations, Ed. 3, Philadelphia, W. B. Saunders Company, 1918, p. 384.

tended to make almost any type of anastomosis successful, many problems remain. As more and more intestinal pediatric surgery is done and more surgery on ducts is carried out, the problems of gathering and hemorrhage continue to be troublesome. When multiple anastomoses are encountered during long operations, the problem of time consumption leads us away from interrupted suture methods, whether they be the meticulous three-layer or the two-layer anastomosis. While most surgeons are satisfied with some simple nonabsorbable interrupted suture for the outer or

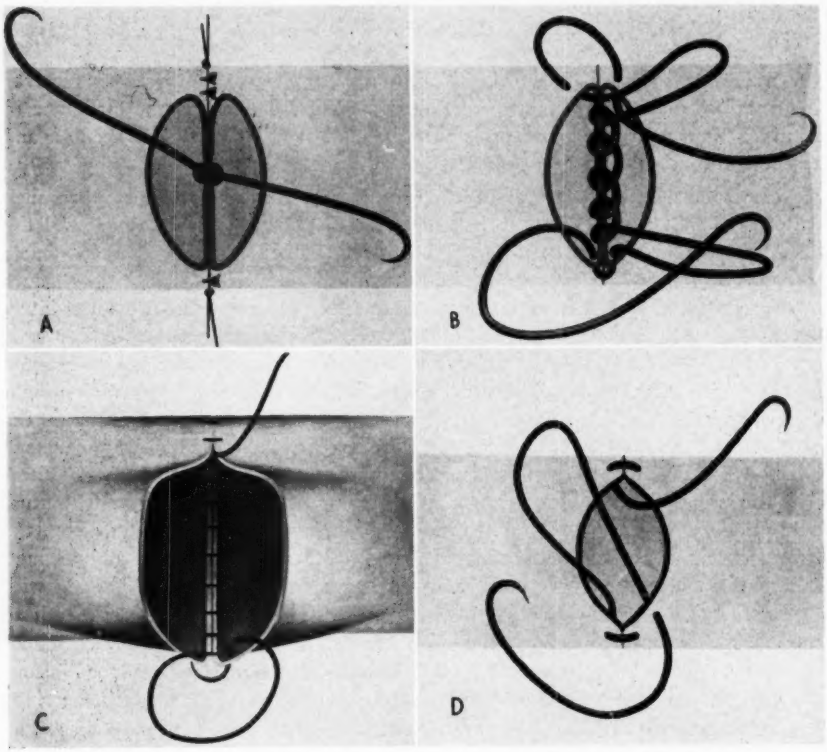

Fig. 1.—*A*, usual posterior layer of seroserous approximation with silk Halsted mattress sutures in place, the ends of the intestine open, and a double-ended fine gastrointestinal suture started in the middle of the posterior layer. *B*, posterior layer of continuous through and through lock stitch completed to each end of the posterior layer. *C*, continuous lock stitch turning the corner at the end of the posterior row. *D*, continuation of this same suture, as a continuous lock suture, having gone "around the corner," and the loop to be held by the assistant or the operator. It is absolutely essential to hold the slack continuously during the entire placing of each suture. Unless this loop is held, the suture may double lock because of twisting or will be lost within the lumen of the anastomosis. The needle is about to be passed through the opposite side.

secondary seroserous layer, the method of handling the anterior primary or inner layer is problematical.

The method presented here concerns only the inner or primary layer and is not set forth as the simplest or as possibly the best method but as a safe and satisfactory one to teach residents as a basic one until they find their own variations. It employs

an anterior extension of the through and through lock or blanket stitch commonly used for the posterior primary or inner layer. This is a simple method to follow, is adaptable to all types and sizes of bowel and duct, but is difficult to illustrate. The lock stitch has a further advantage in that it is most difficult to pull it too tight or leave it too loose.

HOW THE METHOD WAS DEVELOPED

This anastomosis was first evolved in 1940 during an end-to-end iliocolostomy in which considerable discrepancy existed between the diameters of the ends of the

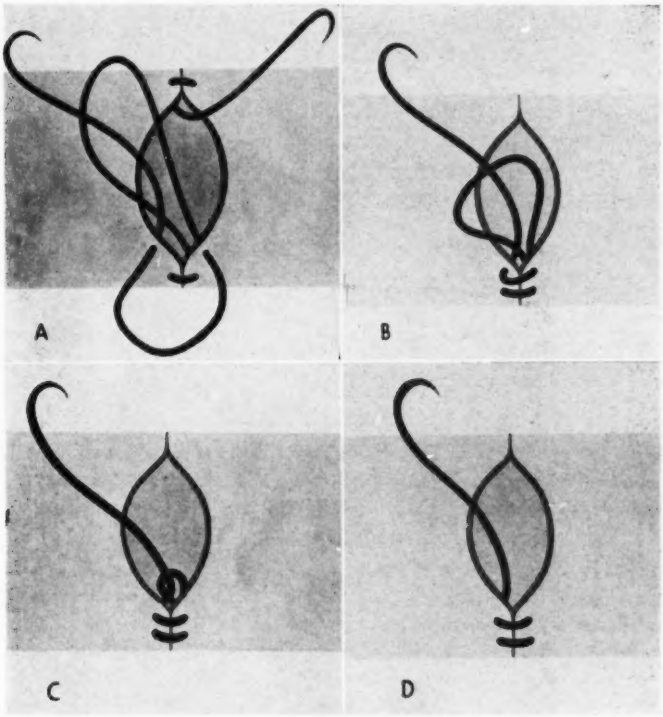

Fig. 2.—*A*, needle is through the opposite side from without in and through the loop to lock the stitch. *B* and *C*, the suture is being drawn up before it disappears beneath the anterior layer within the lumen. *D*, the suture has disappeared to become another "upside down" lock stitch.

colon and the ileum. During the process, attention was so intently focused on the necessary compensating "little and big" stitches that the discovery was suddenly made that the posterior sutures had been "carried too far" and the anterior layer was in fact almost closed. Completion was so easy and simple that the method has been used ever since. It is particularly efficacious in pediatric surgery, in which in the past gathering was such a factor that side-to-side anastomosis had been the rule to avoid stomal constriction. This method, with the fine "watch-like tools" and sutures required for day-old babies, is so adaptable to fine work that end-to-end anastomoses have been made easy, desirable, and accurate. I believe the method

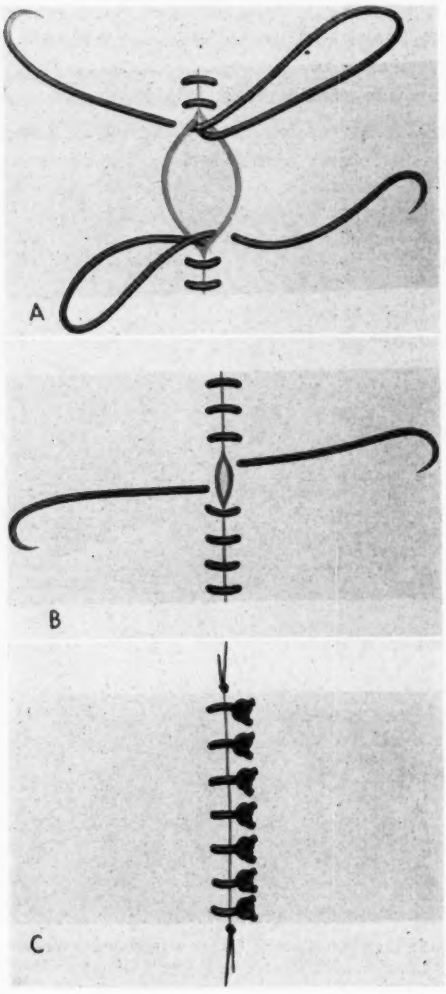

Fig. 3.—*A* and *B*, final progression up to the single last (closing) stitch. Because of the elasticity of the bowel it is possible to insert the suture easily, if the surgeon or his assistant holds the slack for each subsequent lock and if smooth thumb forceps are used to hold the opposing edges of the bowel together for the placing of each stitch. When there is no discrepancy in thickness or elasticity between the two loops being anastomosed, thumb forceps may often hold the anterior edges together and everted sufficiently to place the suture through and through as one motion, the same as in the posterior layer, under direct vision. *C*, final closure is completed, and the anterior layer of serosa to serosa Halsted mattress sutures are in place.

satisfies the desirable requirements of an intestinal anastomosis, and is better than most methods of handling the anterior inner layer for the following reasons: (1) accurate apposition; (2) hemostasis superior to most other inverting sutures; (3) freedom from gathering or stomal constriction; (4) simplicity of performance; (5) avoidance of circulatory interference; (6) adaptability to end-to-end, side-to-side, and end-to-side arrangements with almost any diameter discrepancy or variation in thickness of bowel wall.

METHOD

This method employs a continuous lock stitch, using a single fine chromic gut suture with a needle on both ends. It begins in the middle of the posterior lips of the bowel ends to be approximated after the serous layer approximation with interrupted nonabsorbable sutures has been made and the bowel ends are opened. After continuing to each angle, the suture is carried around each corner and continued to the middle of the anterior layer as an "upside down" lock stitch. The last suture goes from within out on the same side as the lock, to complete the lock. The ends are then tied together. Occasionally when pouting is a problem, one Connell stitch may be desirable. In essence, then, the method embraces the fact that lock stitch can be continued around the anterior layer with the lock within the lumen.

SUMMARY AND CONCLUSIONS

I believe I have shown that this method of handling the inner or primary layer of an anastomosis with this "upside down" lock stitch satisfies the following desirable features:

(1) accurate approximation and inversion; (2) avoidance of gathering and stomal constriction; (3) dependable hemostasis; (4) avoidance of any areas of necrosis due to tension that might interfere with blood supply in uneven spots or cause looseness in other spots that might produce leak or hemorrhage, and (5) simplicity of performance.

For the above reasons I believe this is a good method to teach residents as their first technique of anastomosis until they are able to evolve their own variations in method.

SURGICAL TREATMENT OF POSTIRRADIATION RECTAL STRICTURE AND RECTOVAGINAL FISTULA

E. S. BRINTNALL, M.D.
IOWA CITY

THERE are a number of patients who have been successfully treated for carcinoma of the cervix with radiation therapy in whom rectal strictures and fistulas subsequently develop. It must be kept in mind that rectovaginal fistula may be due to the actual irradiation or to the destruction of neoplasm which has already invaded rectovaginal septum. These complications occur in less than 2% of patients who have received roentgen radiation and radium therapy for cervical cancer.[1] Twelve patients with these complication have been treated at the University Hospital, in Iowa City, during the past two years.

The treatment of these lesions has consisted of resection of the involved rectum and restoration of bowel continuity. The general scheme of treatment is as follows: A proximal colostomy is established, usually in transverse colon, to divert the fecal stream. The rectal segment damaged by irradiation is resected, and bowel continuity is reestablished, most frequently by a low transanal rectal anastomosis. After the rectal anastomosis has healed, the colostomy is closed.

No repair of the vaginal wall or direct attack upon the vaginal portion of the fistula is carried out in patients with rectovaginal fistulas, as vaginal healing occurs spontaneously after the rectum is healed, with an anastomosis located distal to the site of the fistulous vaginal opening.

The 12 patients comprising this series had been treated for carcinoma of the cervix, which when classified in 7 of the patients was considered to represent a League of Nations II or a Schmitz III. The extent of the carcinoma in five instances was not known. Treatment in most of the patients had consisted of a combination of external roentgen radiation and local radium therapy. The Ernst applicator for radium had been used frequently. The amount of radiation therapy given was not considered to be excessive, nor did the technique utilized appear to be concerned. The radiation therapy had been administered in several different hospitals and under the supervision of several different radiologists.

Rectovaginal fistulas in nine patients appeared from 1 to 15 months after the completion of radiation therapy, the average interval being 11 months. In 2 of these nine patients, both vesicovaginal and rectovaginal fistulas developed.

Rectosigmoid colon strictures appeared in the other three patients, at 1 month, 15 months, and 9 years after irradiation.

From the Department of Surgery, State University of Iowa, College of Medicine.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 6, 1953.

1. Kerr, H. D., and Elkins, H. B.: Unpublished data.

All patients with fistulas had biopsies carried out before consideration was given to repair of the fistulas.

Inasmuch as the radiation effects included impaired vascularity of tissue in and near the area of obvious injury, a wide excision of tissue was thought to be necessary to provide vascular tissues for healing after repair. Thus very low rectal anastomoses had to be utilized.

Anterior (transabdominal) anastomosis of the rectum was possible in only two instances of rectosigmoid stricture. The rectal anastomoses in these two patients were located 5 and 7 cm. above Hilton's white line. Healing and complete fecal continence resulted in both patients (M. D. and A. Mc.).

Abdominal-perineal "pull-through" procedures (Hochenegg's operation) were utilized in three instances for rectovaginal fistulas of large size. One of these patients (G. B.) died two months after operation of sepsis and inanition. This patient also had a large vesicovaginal fistula and partially obstructed ureters. In

*Surgical Treatment of Irradiation Rectal Lesions**

Patient	Age, Yr.	Type of Irradiation	Interval, Mo.	Lesion	Reconstruction	Result
V. B.	35	Ext. x-ray and radium	9	R fist.	Transanal	Good
M. D.	64	Ext. and transvaginal x-ray	9 yr.	Stricture	Abdominal	Good
G. S.	42	Ext. x-ray and radium	11	R fist.	Transanal	Good
F. G.	50	Ext. x-ray and radium	15	R fist.	Pull-through	Fair
R. L.	39	Ext. x-ray and radium	1	Stricture	Transanal	Good
C. B.	46	Ext. x-ray and radium	15	R fist. V fist.	Transanal Ileal bladder	Good
G. B.	54	Ext. x-ray and radium	15	R fist. V fist.	Pull-through	Died
H. K.	54	Ext. x-ray and radium	12	R fist.	Pull-through	Fair
L. W.	33	Ext. x-ray and radium	1	R fist.	Transanal	Good
L. J.	36	Ext. x-ray and radium	15	R fist.	Perineorrhaphy	Failure
A. Mc.	75	Type not known	15	Stricture	Abdominal	Good
F. H.	43	Ext. x-ray and radium	9	R fist.	Transanal	Good

* The following abbreviations are used: Ext., external; R fist., rectovaginal fistula; V fist., vesicovaginal fistula.

retrospect, her death does not seem to be a direct result of the operation, but rather a result of the extensive radiation tissue injury. The other two patients (F. K. and H. K.) treated by pull-through with preservation of external anal sphincter and suture of sigmoid to anal skin are well and free of fistula but are not completely continent. Their degree of continence is estimated to be one-third to one-half of normal. Much of their difficulty can be attributed to loss of anal canal sensation, though in each patient there is also marked diminution in anal sphincter tone. Each patient is able, however, voluntarily to tighten the sphincter strongly for short periods of time. These two patients live more comfortably than they did with colostomies but do not represent ideal results of treatment. It is believed that the abdominal-perineal pull-through procedure should not be carried out when bowel continuity can be reestablished by transanal anastomosis.

In one patient (L. J.) with rectovaginal fistula the vaginal and rectal tissues near the small fistula seemed so pliant and vascular that careful local excision of the fistula and repair were carried out after a preliminary colostomy. Despite a two-layer repair of rectum with a transverse suture line and vaginal closure (perineorrhaphy) with a vertical line of repair, there was a recurrence of the fistula

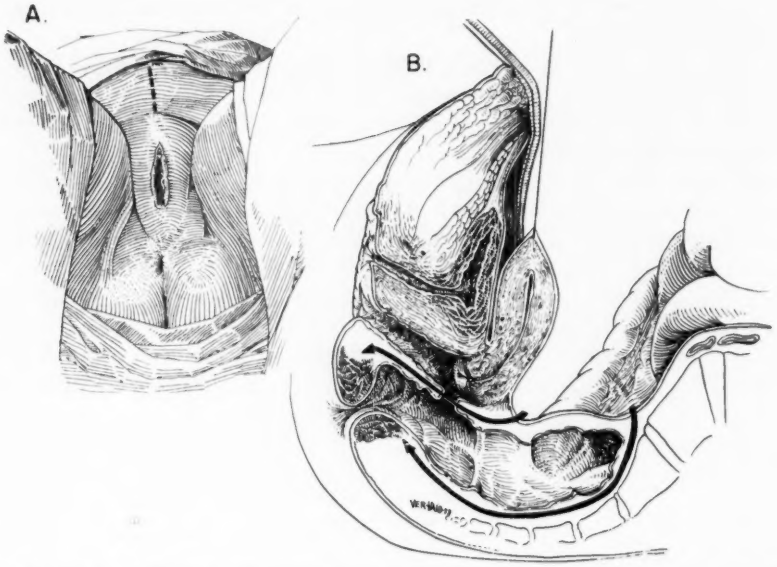

Fig. 1.—Lower abdomen and perineum are prepared and draped in continuity. *A*, midline lower abdominal incision. *B*, arrows indicating planes of dissection.

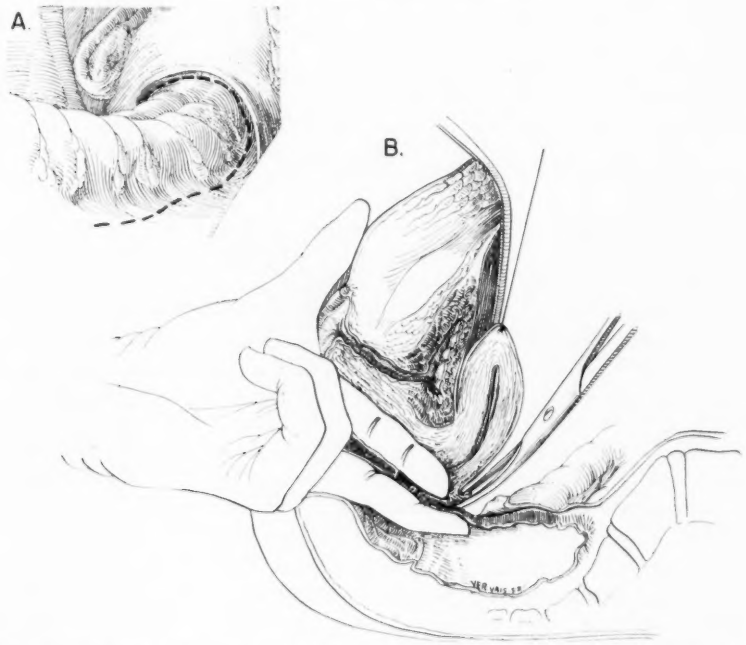

Fig. 2.—*A*, line of peritoneal incision in pelvis and cul-de-sac. *B*, method of dissection in rectovaginal septum.

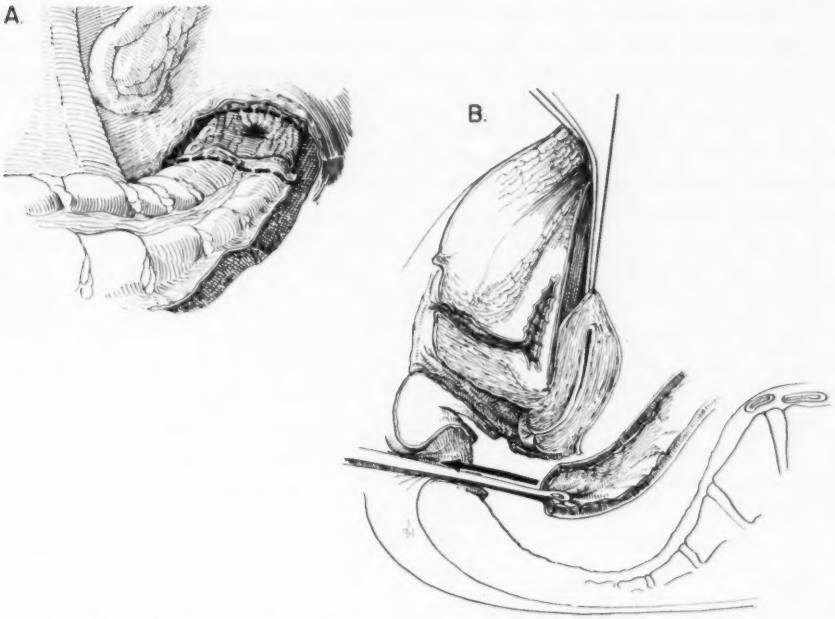

Fig. 3.—*A*, lines indicating levels of resection of damaged segment of rectum. *B*, proximal rectum being drawn through anus.

Fig. 4.—Anal segment is everted and proximal rectum telescoped through anus. A two-layer anastomosis is accomplished with interrupted nonabsorbable surgical (fine silk) and absorbable surgical (gut) sutures.

shortly after operation. The discouraged patient will not permit another operation (resection and transanal anastomosis have been proposed to her). The failure in this case illustrates the futility of attempting local transvaginal repairs of post-irradiation fistulas.

In one patient (R. L.) with irradiation stricture and in five patients (V. B., G. S., C. B., L. W., and F. H.) with irradiation rectovaginal fistulas, treatment consisted of abdominal resection of the involved segment of rectum and restoration of bowel continuity by an eversion transanal-type anastomosis, as illustrated in Figures 1 to 5. This procedure embodies the essential technical principles popularized by Swenson [2] for the treatment of megacolon. Each patient had had a preliminary proximal colostomy, usually located in the right half of the transverse colon and usually with divided and separated limbs to divert the fecal stream

Fig. 5.—Completed anastomosis is allowed to retract upward. Pelvic reperitonealization is carried out.

completely and to permit a more effective cleansing of the distal colorectal segment of bowel. Resection and anastomosis were not undertaken until the colostomy had been present for several months, until maximal improvement of tissues adjacent to the fistula had occurred. In one of these six patients (C. B.) a large vesicovaginal fistula was also present, the bladder trigone and bladder-neck sphincter having been destroyed by the slough. In this patient an ileal bladder was constructed in the manner advocated by Bricker [3] and a transverse colon colostomy set up five months prior to resection of the rectum and transanal anastomosis. The rectal fistula has healed; the patient is completely continent of feces, and the ileal bladder functions

2. Swenson, O.: New Surgical Treatment for Hirschsprung's Disease, Surgery **28**:371-383 (Aug.) 1950.

3. Bricker, E. M.: Symposium on Clinical Surgery: Bladder Substitution After Pelvic Evisceration, S. Clin. North America **30**:1511-1521 (Oct.) 1950.

satisfactorily and is well tolerated by the patient. In the immediate preoperative period all patients are prepared for operation by cleansing of both the defunctionalized bowel segment and the vagina and by instillation of solutions containing appropriate antibiotics. The six patients treated by resection of rectum and transanal anastomosis have recovered completely. There has been no recurrence of fistula and no rectal incontinence. The anastomoses were located at very low levels, varying from 1 to 3 cm. above Hilton's white line (pectinate or dentate).

The technique of resection and low transanal anastomosis is illustrated step by step in Figures 1 to 5. A suprapubic midline incision is utilized for the abdominal mobilization of the rectum and for reperitonealization in the pelvis after the perineal transanal anastomosis is completed. The patient is positioned in stirrups, and the abdomen and perineum are prepared and draped as one operative field to facilitate the operator's dissection with one hand, while the fingers of his other hand in the rectum and vagina serve as guides in freeing the rectum and anal canal from the vagina. This maneuver is important because distinct cleavage planes between the rectum and the vagina have been obliterated by inflammation and scarring. The fistulous vaginal opening is not disturbed and no posterior wall vaginal incision is made for fear of superimposing vaginal repair upon a low bowel anastomosis with consequent likelihood of anastomotic leak and recurrence of fistula.

Colostomy closure after resection and reestablishment of bowel continuity by any of the aforementioned methods is usually carried out after a period of 2 or 3 months, sufficient time having elapsed to make security of healing certain.

SUMMARY

Twelve patients with rectovaginal fistula or rectosigmoid stricture subsequent to radiation therapy of carcinoma of the cervix were treated surgically. One patient died two months after operation. In one patient a recurrence of the rectovaginal fistula developed after transvaginal repair. Two patients are well but only partially continent of feces after pull-through (Hochenegg) procedures. Of the remaining eight patients, two were treated by anterior resection and anastomosis and six by resection and transanal anastomosis, with healing and complete fecal continence. An ileal bladder was constructed in one patient with an associated vesicovaginal fistula.

The technique of low transanal rectal anastomosis is described.

DISCUSSION

DR. LEON S. MCGOOGAN, Omaha: I wish to thank Dr. Brintnall for bringing to this group a method of handling one of the most difficult and serious complications in the use of radium and deep x-ray therapy in the management of carcinoma of the cervix. The fact that such a complication does occur in no way invalidates the use of radium and deep x-ray therapy, but does propose the question of why it occurs. What can be done to prevent the occurrence of this complication?

In the last two decades there has been a gradual increase in the amount of radiation used in the treatment of carcinoma of the cervix. However, we have learned with our use of radium that the concentration of the dose should be less in the region of the cervix and more in the region of the fundus and in the lateral vaults of the vagina so that the lateral areas of the cervical region are treated and a less concentrated dose is directed toward the rectum.

shortly after operation. The discouraged patient will not permit another operation (resection and transanal anastomosis have been proposed to her). The failure in this case illustrates the futility of attempting local transvaginal repairs of post-irradiation fistulas.

In one patient (R. L.) with irradiation stricture and in five patients (V. B., G. S., C. B., L. W., and F. H.) with irradiation rectovaginal fistulas, treatment consisted of abdominal resection of the involved segment of rectum and restoration of bowel continuity by an eversion transanal-type anastomosis, as illustrated in Figures 1 to 5. This procedure embodies the essential technical principles popularized by Swenson [2] for the treatment of megacolon. Each patient had had a preliminary proximal colostomy, usually located in the right half of the transverse colon and usually with divided and separated limbs to divert the fecal stream

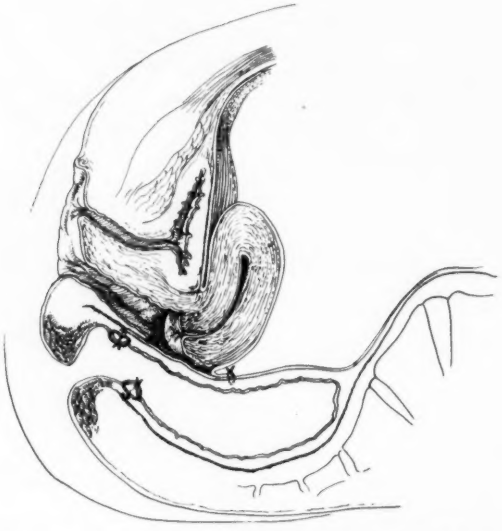

Fig. 5.—Completed anastomosis is allowed to retract upward. Pelvic reperitonealization is carried out.

completely and to permit a more effective cleansing of the distal colorectal segment of bowel. Resection and anastomosis were not undertaken until the colostomy had been present for several months, until maximal improvement of tissues adjacent to the fistula had occurred. In one of these six patients (C. B.) a large vesicovaginal fistula was also present, the bladder trigone and bladder-neck sphincter having been destroyed by the slough. In this patient an ileal bladder was constructed in the manner advocated by Bricker [3] and a transverse colon colostomy set up five months prior to resection of the rectum and transanal anastomosis. The rectal fistula has healed; the patient is completely continent of feces, and the ileal bladder functions

2. Swenson, O.: New Surgical Treatment for Hirschsprung's Disease, Surgery **28**:371-383 (Aug.) 1950.

3. Bricker, E. M.: Symposium on Clinical Surgery: Bladder Substitution After Pelvic Evisceration, S. Clin. North America **30**:1511-1521 (Oct.) 1950.

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This is also true of deep x-ray therapy, in which the dose was formerly directed with concentrated converging doses into the region of the rectum, but now has to be concentrated to the lateral walls of the pelvis.

In the placement of radium, the position of the radium should be such that its placement can be checked with either anterior-posterior or lateral x-rays, or preferably with both.

Dr. Franklin Payne, of the University of Pennsylvania, devised a most ingenious method for postoperative estimation of the placement of the radium capsules in the cervix and in the lateral vaults. Placement can be maintained to a certain extent if packing is used in the vagina, but the packing should be of a plastic type, such as gauze soaked with boric acid ointment or with barium sulfate, which creates a plastic mass that holds the radium in the right position so that it cannot slip.

We have used this particular method at the University of Nebraska College of Medicine, but we have gone one step further, in which we regulate the dose of radium so that if the placement is wrong on the first attempt and discovered at a little later date, the damage to the rectum cannot be too great, and the subsequent placement can be more accurate.

I want to reemphasize that radium and deep x-ray therapy are still the treatments of choice for carcinoma of the cervix, that radium and deep x-ray therapy still show better results than surgery in the treatment of carcinoma of the cervix, and that the complications—such as have been presented today—should in no way deter us from continued use of radium and deep x-ray therapy.

The tendency toward a greater use of surgery, except in a very, very limited field, should be curtailed.

POLYPS OF THE COLON

Late Results of Transcolonic Removal

EDWARD S. JUDD Jr., M.D.
AND
JOHN C. CARLISLE, M.D.
ROCHESTER, MINN.

PEDUNCULATED polyps of the large intestine have been the subject of numerous clinical studies, of many arguments among pathologists, and of some philosophic speculation, especially in the last two decades. Continuing interest in this subject is kept alive by the inescapable fact that final proof regarding the exact life history and potentialities of a given polyp of the large intestine has not been forthcoming. It follows that differences of opinion still exist concerning proper treatment for this most interesting lesion.

It is surprising to note in the voluminous literature that late results of treatment in significant series of cases are not available; much of the confusion still prevalent stems from the fact that speculation and philosophy have far outdistanced scientific fact. We do not care to belabor the point concerning whether polyps are all benign or all malignant or whether they are commonly or rarely the precursors of carcinoma. We are vitally interested, however, in an attempt to demonstrate whether colotomy with excision of a pedunculated polyp is adequate treatment. It logically follows that we must ask whether the presence of multiple polyps would change a preexisting viewpoint. Recent tremendous strides made in colonic surgical techniques obviously stimulate consideration as to whether more radical treatment should be offered for what previously was thought to be a less serious lesion. Whereas in most medical centers today segmental resection of almost any portion of the colon is carried out with small risk to the patient, conscientious surgeons must ask whether any increase in risk in the treatment of this lesion is actually worth while for the patient.

REVIEW OF LITERATURE

Polyps of the Entire Colon.—McLanahan and his associates [1] pointed out that conflict existed regarding the relation of adenomatous polyps to actual carcinoma. In 1931 Fitzgibbon and Rankin [2] stated that it should be possible to discriminate

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Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 6, 1953.

1. McLanahan, S.; Grove, G. P., and Kieffer, R. F., Jr.: Conservative Surgical Management for Certain Rectal Adenomas Showing Malignant Change, J. A. M. A. **141**:822-825 (Nov. 19) 1949.

2. Fitzgibbon, G., and Rankin, F. W.: Polyps of the Large Intestine, Surg., Gynec. & Obst. **52**:1136-1150 (June) 1931.

histologically between those polyps which would develop into cancers and those which would pursue an entirely benign course. It is interesting to note that David,[3] in 1934, argued against the potential malignant growth of adenomatous polyps. He reasoned that benign polyps of the colon were found frequently at necropsy; he stressed a second point, namely, that it was not too unusual to find polyps in children, whereas colonic carcinoma in children was extremely rare.

More recently, most authors have turned toward the opinion that regardless of the picture presented by the microscopic section of a polyp a potentiality for malignant change exists; most authorities admit at present that there is no way to tell, microscopically, which polyps may be progressing toward the carcinomatous stage. In 1935 Buie and Brust [4] reported on eight patients who had "solitary adenoma of the colon" and who refused treatment. Definite clinical carcinoma developed in four of these patients at the sites of the original polyps during periods varying from 2 to 10 years. Swinton and Warren [5] made a pathologic study of 827 patients who had carcinoma of the colon and concluded that the cancer had started in a polyp in 14%. They also studied 156 patients who had so-called benign polyps and announced that all stages in the sequence of change from normal mucosa to adenocarcinoma could be demonstrated histologically. A distinct general trend to this same view is noted in many more recent articles.

Helwig [6] disagreed with Fitzgibbon and Rankin; he stated that "no evidence could be adduced that any particular group of adenomas would maintain a constant benign course." Helwig concluded that whereas some colonic cancers develop from previously normal mucosa, the great majority have adenomas as their precursors. Atwater and Bargen [7] were of the opinion that the term "polyp" represented only one stage in the development of a colonic lesion that sooner or later would reveal unquestionable evidence of malignant growth. In 1949 Buie [8] added that "all polyps of the colon are cancers or will become cancers if they are not destroyed and if the patient lives long enough."

In 1951 Rankin and Conger [9] agreed that "most carcinomas of the large bowel originate in polyps or have polyps as their earliest manifestations." Kennedy and his associates,[10] as well as Kerr,[11] were of the opinion that polyps in children are usually benign. Kerr went on to present a study of 100 children who had polyps, and he reported that the lesions did not show the early malignant changes histo-

3. David, V. C.: The Pathology and Treatment of Bleeding Polypoid Tumors of the Large Bowel, Ann. Surg. **100**:933-948 (Nov.) 1934.

4. Buie, L. A., and Brust, J. C. M.: Solitary Adenomata of the Rectum and Lower Sigmoid, Tr. Am. Proct. Soc. **36**:57-65, 1935.

5. Swinton, N. W., and Warren, S.: Polyps of the Colon and Rectum and Their Relation to Malignancy, J. A. M. A. **113**:1927-1933 (Nov. 25) 1939.

6. Helwig, E. B.: The Evolution of Adenomas of the Large Intestine and Their Relation to Carcinoma, Surg., Gynec. & Obst. **84**:36-49 (Jan.) 1947.

7. Atwater, J. S., and Bargen, J. A.: The Pathogenesis of Intestinal Polyps, Gastroenterology **4**:395-408 (May) 1945.

8. Buie, L. A.: Polypoid Disease of the Colon, Postgrad. Med. **5**:177-183 (March) 1949.

9. Rankin, F. W., and Conger, A. B., Jr.: Metachronous Carcinomas of the Colon, J. A. M. A. **146**:918-920 (July 7) 1951.

10. Kennedy, R. L. J.; Dixon, C. F., and Weber, H. M.: Polypoid Lesions of the Colon of Children, Surg., Gynec. & Obst. **77**:639-644 (Dec.) 1943.

11. Kerr, J. G.: Polyposis of the Colon in Children, Am. J. Surg. **76**:667-671 (Dec.) 1948.

logically characteristic of those in polyps in the adult colon. Kerr did admit, however, that in two cases of carcinoma in children, the malignant lesion appeared most likely to have developed at the exact site of previously known polyps that had not been removed.

Polyps Beyond Reach of the Sigmoidoscope.—Both Boyd [12] and Swinton [13] commented on the relative incidence of polyps in the colon as well as the rectum. Boyd earlier had stressed the incidence of polyps in the upper reaches of the colon in patients more than 40 years of age. Buie,[8] in a study of patients who did not have signs or symptoms referable to the colon, found a surprisingly large incidence of polyps beyond reach of the sigmoidoscope. Swinton and Holt [14] discovered that the polyps presented above the proctoscopic level in nearly 20% of their cases. Scarborough and Klein,[15] as well as DeMuth and his associates,[16] stressed the importance of a search for multiple polyps when one polyp had been demonstrated; this principle appears to be accepted in most current articles.

PRESENT PROBLEM

Most authorities now agree that a polyp in the large intestine is a signal of danger. At the risk of oversimplification, the problem presents itself as one of a decision at the time of surgical treatment as to just how much operative intervention is actually indicated. Without entering a controversy concerning whether a given polyp does or does not show malignant changes, we are completely convinced that a colon in which polyps are prone to form serves warning that it is also a colon in which carcinoma is prone to form. It would be instructive to know what the mucosa between polyps will reveal many years later, but no method has been developed to predict this.

The association of "sentinel polyps" in the same specimen with "full-blown" colonic cancers has been striking; possibly the presence of two or more polyps renders the patient who harbors them more susceptible to the development of cancer. In the voluminous literature it was most disappointing to find no long-term follow-up studies on patients who had previously undergone transcolonic polypectomy. It was therefore decided that it would be worth while to attempt to determine the fate of patients who had been subjected to this operation.

MATERIALS AND METHODS

The records of patients who had undergone laparotomy at the Mayo Clinic with removal of a polyp or polyps from the colon by the so-called transcolonic method were reviewed. All cases that could possibly be listed as "multiple polyposis" or "familial polyps" were carefully avoided. Those cases in which frank carcinoma of

12. Boyd, C. E.: Polyps of the Colon, New Orleans M. & S. J. **104**:92-96 (Sept.) 1951.

13. Swinton, N. W.: Diagnosis and Treatment of Mucosal Polyps of the Rectum and Colon, with Early Malignant Change, Am. J. Surg. **75**:369-373 (Feb.) 1948.

14. Swinton, N. W., and Holt, J. H.: Polyps of the Colon and Rectum, in Surgical Practice at the Lahey Clinic, Philadelphia, W. B. Saunders Company, 1951, pp. 391-405.

15. Scarborough, R. A., and Klein, R. R.: Polypoid Lesions of the Colon and Rectum, Am. J. Surg. **76**:723-727 (Dec.) 1948.

16. DeMuth, W. E., Jr.; Cherney, P. J., and Fitts, W. T., Jr.: Adenomatous Polyps of the Colon and Rectum: A Challenge in Cancer Prophylaxis, Surg., Gynec. & Obst. **94**:195-199 (Feb.) 1952.

the colon coexisted or might possibly have existed at the time of admission were eliminated. This left a consecutive series of 246 cases as of Jan. 1, 1947. Follow-up studies were begun Jan. 1, 1952, affording a minimal period of five years. The usual complete history and physical examination were noted with interest, but the chief criteria were proctoscopic studies and roentgenologic examinations of the colon. In the great majority of cases, these studies were done at frequent intervals, when the patient returned to the clinic. In a few instances, reliable reports from proctologists and roentgenologists in the patient's home city were included as part of the permanent record. The remainder of the study was conducted by means of the customary follow-up letters, which incorporated reports of the home physician.

It was gratifying to note that 98% of patients returned as instructed for follow-up visits during the first two years after operation; the five-year follow-up rate was 95%. This was interpreted to mean that the patients had been sufficiently impressed with the gravity of the potentialities that they heeded the warnings and returned on schedule. It was therefore all the more surprising and disappointing to find that the 10-year follow-up rate was but slightly more than 40%. It can only be assumed from the latter that a large number of patients decided for themselves

TABLE 1.—*Over-All Results of Transcolonic Excision in 246 Cases of Polyps of the Colon*

Result	Cases	
	No.	%
No further polyps	177	72
Further polyps requiring abdominal operation	37	15
Further polyps requiring fulguration	32	13

that having remained free of polypoid disease or, perhaps, having been treated for further polypoid disease and having been pronounced well at the end of five years, they would discontinue further investigation.

RESULTS

The over-all results in the entire group of 246 patients are summarized in Table 1. It is immediately apparent that in a résumé of this type, one cannot be certain whether further polypoid disease represents a recurrence at exactly the same site or whether it merely means development of an entirely independent polyp in the same general region of the colon. Without attempting to be arbitrary, we analyzed the records as critically as possible and believe that in most cases it is now apparent to us whether or not we are dealing with true recurrence.

Proceeding on this basis, we then attempted to analyze various factors to see whether a common denominator might be determined to help detect those patients who might be destined to have recurrence.

Age and Sex.—As might be expected, 77% of the cases occurred in patients who were in the fifth, sixth, or seventh decade of life. Almost none were encountered in children, and few were found before the fourth decade of life. No difference at all was found between the ages of patients who had recurrence and those who did not.

Contrary to findings of other authors, only 54% of our patients were males; of those who experienced further polypoid disease and required laparotomy for definitive treatment, only 47% were males.

Histopathology.—Close scrutiny of the pathologists' records disclosed consistent use of terminology that allowed rather clear-cut definition of the histologic picture. Four categories suffice to include all the polyps: (1) adenomatous polyps (Fig. 1);

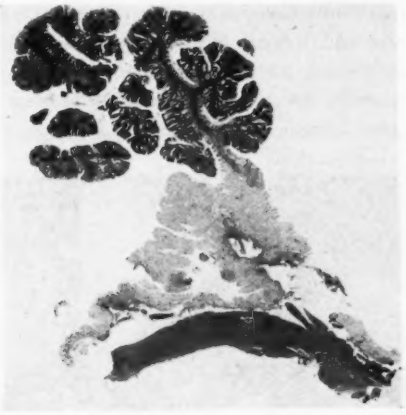

Fig. 1.—Typical pedunculated adenomatous polyp. A single lesion of this type ordinarily is cured by transcolonic excision (hematoxylin and eosin; × 2).

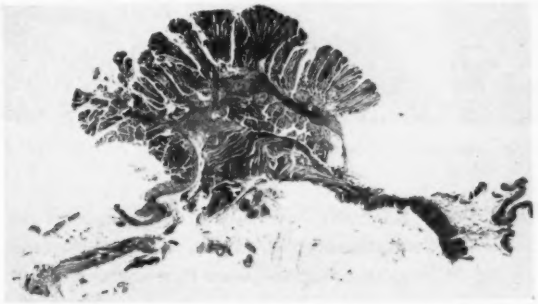

Fig. 2.—Adenomatous polyp with malignant changes of invasive type; transcolonic excision of these lesions is followed frequently by recurrence (hematoxylin and eosin; × 1.5).

(2) adenomatous polyps with low-grade noninvasive adenocarcinoma (carcinoma in situ); (3) adenomatous polyps with low-grade invasive carcinoma (Fig. 2), and (4) carcinomatous polyps (Fig. 3).

One consistent difference between the third and fourth groups was that the lesion in the latter was obviously malignant grossly.

In the final analysis of cases in which additional polyps developed after transcolonic excision, it was found that recurrent lesions which were definite clinical adenocarcinomas were present in 50% of cases in which the original polyp was

reported to reveal definite evidence of microscopic invasion. In the entire group of cases, there were 15 recurrent lesions that were obviously malignant. All but one of those which recurred at a level identical with that of the original polyp presented the microscopic picture of low-grade carcinoma with invasion of the stalk. The original lesions in those patients in whom further polyps occurred at an entirely different level of the colon all showed no evidence of invasion.

Location of Original Polyp.—As might be predicted, the great majority of the polyps removed by transcolonic excision were in the sigmoid and descending colon. Table 2 presents a correlation of the location of the new polyp with that of the original lesion. It is interesting that although many polyps were seen by the proctologist, in at least 12 patients the proctologist did not attempt treatment but sought the services of the surgeon because of the nature of the disease.

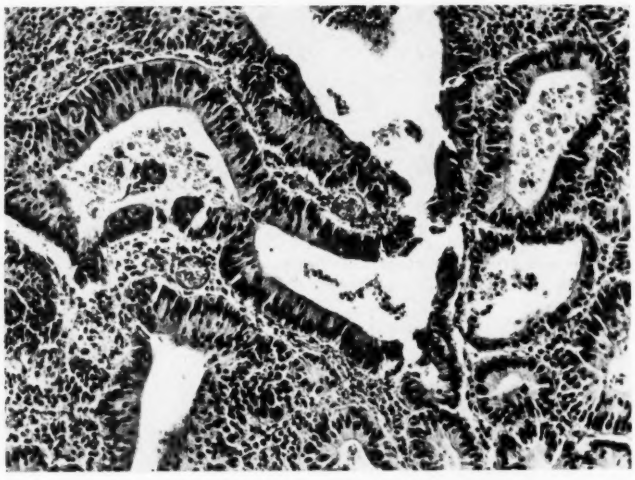

Fig. 3.—Carcinomatous polyp; this type of lesion requires resection of the colon (hematoxylin and eosin; × 150).

It is noteworthy that a relatively high rate of recurrence of polyps was noted in that portion of the large intestine located within 20 cm. of the anal opening. This is consistent with the findings of other authors. It is apparent from Table 2, also, that a relatively high rate of recurrence is present in the colon on the right side. It might be argued that the small size of this series renders this observation insignificant, but the fact remains that recurrent polyps were found largely in regions identical with those of the original lesions.

Number of Polyps at Original Operation.—Of the entire group of patients, 60% had definitely single, isolated polyps and 15% possessed three or more polyps at the time of original examination. Of the patients who suffered from recurrent or new polypoid disease, 25% originally had three or more polyps. A more detailed analysis of this feature is presented in Table 3. It would appear that a patient who had four or more polyps originally has a much greater chance of incurring further polypoid

disease than does the person who has a single polyp at the first examination. It may be that patients who had multiple polyps were subjected to much closer scrutiny after the first polyps were discovered, as it was noted that some of the polyps found at follow-up examination could be treated by fulguration. The fact remains that definite trends toward recurrence of polyps were apparent in these patients.

Time Interval Before Recurrence.—Recurrent polyps (or perhaps new polyps) appeared at variable periods. Such polyps were found at periods ranging from 10 months to more than 13 years after the transcolonic excisions done at the clinic. Of the 15 obviously malignant recurrent lesions, 4 had appeared within the first

TABLE 2.—*Location of First Polyp and That of New or Recurrent Lesion in 246 Cases*

Location of Original Lesion	Cases, No.	Location of New or Recurrent Polyp: Abdominal Operation Required, Cases No.	%	Treated Proctoscopically, Cases No.	%	No Further Disease, Cases No.	%
Proctoscopic region (last 20 cm. of large intestine)	12	4	33	3	25	5	42
Sigmoid	145	16	11	17	12	112	77
Descending colon	70	12	17	9	13	49	70
Transverse colon	11	2	18	0	0	9	82
Ascending colon	8	3	37.5	3	37.5	2	25
Total	246	37	..	32	..	177	..

TABLE 3.—*Relation of Number of Polyps to Recurrence in 246 Cases*

Original Polyps, No.	Cases, No.	Further Polyps in Same Region, Cases No.	%	No Further Polyps, Cases No.	%
1	147	38	26	109	74
2	62	13	21	49	79
3	16	3	19	13	81
4	9	5	56	4	44
5	4	3	75	1	25
More than 5	8	6	75	2	25

year, whereas 1 required 13 years. The average time elapsed before recurrence was noted in these cases was four and seven-tenths years.

Twenty-one "benign" polyps recurred above the level of the rectosigmoid; seven of these had appeared within 1 year, whereas in one case 12 years went by before a polyp could be found. The average time elapsed before recurrence was noted in these cases was three and nine-tenths years. In 9 of the 32 patients in whom polyps recurred in the rectosigmoidal region, where they could be seen easily with the proctoscope, such polyps had developed within the first year; this led to the conclusion that in many cases these were definitely new lesions. The other recurrences in this group appeared at various times, the longest period being 12 years. In this particular group, the average time required for development of additional polyps was three and one-half years.

Postoperative Mortality.—Only 2 postoperative deaths occurred in the entire group of 246 patients who underwent colotomy and excision of the polyps. One death occurred in 1920, and one in 1941. In both cases, death was caused by generalized peritonitis.

Analysis of Deaths in Follow-Up Period.—During the years covered by the follow-up study, it was found that death had occurred in 10 cases in which polyps had recurred above the rectosigmoidal level; all these deaths were apparently related to the original disease. Of tremendous importance is the fact that in seven of these cases death was due to carcinoma of the colon. In 2 other instances, it is extremely likely that carcinoma of the colon was the cause of death; in the 10th case, death resulted from a surgical attempt to correct a fecal fistula one year after the transcolonic operation. Of this group of 10 patients, only 5 were alive more than five years after transcolonic polypectomy.

Only four deaths have occurred in patients in whom polyps recurred in the large intestine distal to the sigmoidal region; however, it is extremely important to note that one of these patients died because of carcinomatosis and one because of complete obstruction of the colon. The other two patients died of entirely unrelated causes.

Death occurred in 28 patients who had no known recurrence. Approximately two-thirds of these patients had lived more than 5 years and one-third more than 10 years after transcolonic polypectomy. It was of great interest to learn that 14 of the patients died of causes entirely unrelated to the polyps, 12 of causes presumably unrelated, and but 2 of possibly related causes, namely, "cancer, site undetermined."

COMMENT

Before this study was begun, it was obvious that no infallible method could be developed to predict the future of a given patient who had a polyp of the colon; however, it was gratifying to find certain criteria that tend to warn regarding recurrence of polyps or development of colonic carcinoma. It was pleasing to note the great number of 5-year follow-ups, but, as the study progressed, we became deeply impressed with the necessity of 20-year or 30-year follow-up studies, since nearly a third of all recurrences made their appearance after the first interval of 5 years.

The most important factor with regard to malignant recurrence was whether or not microscopic evidence of invasion was reported in the original polyp. Definite clinical carcinoma could be traced to such a change in an appreciable number of cases. The great majority of these carcinomas appeared to have developed at the identical level at which the original polyp had been removed. Obviously, any polyp that reveals microscopic evidence of invasion is inadequately treated by simple transcolonic excision.

Two additional factors of prime importance were the location of the original polyp and the total number of polyps at the first examination. Polyps that occurred in the region of large intestine visible to the proctologist were prone to recur in a surprising number of patients. It cannot be stated with certainty whether or not these so-called recurrences are new polyps, but we are of the opinion that the colon which is capable of producing polyps in this segment is prone to continue this unhealthy tendency; since the proctologist can easily see this region, such examination can reveal accurate information at an early date. The reason for transcolonic

excision of some of these polyps was that the proctologist was unwilling to assume responsibility for their treatment because of the size, fixation, or general gross appearance of the lesions. More consideration should be given to so-called low anterior resection for polyps in the rectosigmoidal region.

The other portion of the large intestine where recurrence of polypoid disease was common was the descending colon and that part of the colon proximal to it. In this part of the colon, 3 of 10 recurrent polyps treated surgically were located at exactly the same level as the original lesion. All but 2 of the 10 patients would probably have had no recurrence if segmental resection or subtotal colectomy had been performed. Such resection would often require removal of the distal half of the transverse colon, the splenic flexure, all of the descending colon, and much of the sigmoid. This is an extensive operation for a lesion that some authorities still insist is benign; it may be questioned whether even this would be sufficient to guarantee complete protection, since enough colon is still preserved for the development (at least theoretic) of other polyps later. During the early years included in this study, the postoperative mortality rate for segmental resection was perhaps 9%. In more recent years, a satisfactory decrease to approximately 2 or 3% has taken place; however, this is still considerably different from the postoperative mortality rate of 0.8% associated with transcolonic excision.

Evidence of subsequent development of polyps somewhere in the colon was noted in about two-thirds of those cases in which four or more polyps, including those seen by the proctologist, were present at the original examination; abdominal operation was required for at least one such polyp in the majority of cases. If only the number of polyps originally present above the level of the rectosigmoid in patients is considered, it is alarming to note that more than half of such patients revealed evidence of other polyps somewhere in the large intestine at a later time.

Review of the factor of "surgical recurrences" focuses attention on serious consideration of extensive segmental resection or actual subtotal colectomy as the operation of choice in the future. This is especially true for any region in the abdominal portion of the large intestine where two or more polyps are relatively close together. We are of the opinion that in these cases this entire segment of large intestine should be removed; a much more extensive resection probably will guarantee the patient a future far more nearly free of polypoid disease than will less radical procedures.

SUMMARY AND CONCLUSIONS

Follow-up study has been carried out in 246 consecutive cases in which transcolonic excision of polyps of the colon had been performed at the Mayo Clinic at least five years previously.

Only a single polyp was present in approximately 60% of the cases, whereas three or more polyps were found in 15%.

Additional polyps developed later somewhere in the large intestine in 28% of the entire group.

Definite clinical carcinoma of the colon appeared later in 15 patients of the entire series.

More than 50% of those polyps in which microscopic evidence of invasion of malignant cells was present recurred as clinical carcinoma. It is our opinion that such polyps should be treated originally as definite carcinoma.

Further abdominal operations were required for recurrent polypoid disease in 48% of patients in whom four or more polyps were present at the original examination and in whom transcolonic excision was the only surgical procedure.

In the majority of cases in which secondary surgical intervention was required, the recurrent polyp was either at the same site as the original one or between that site and the rectosigmoidal level. Only 5 of 36 so-called surgical recurrences appeared proximal to the midportion of the transverse colon.

It is recommended that more serious consideration be given to extensive segmental resection or subtotal colectomy, especially in view of the steady improvement in surgical methods at present.

DISCUSSION

DR. R. K. GILCHRIST, Chicago: Many proctologists here have ideas on this subject.

I have been using a proctoscope of smaller diameter in these cases to inspect the open bowel through the abdomen.

I had one patient in whom I finally resected the colon from the hepatic flexure to the rectum and then did an anastomosis between the hepatic flexure and the rectum. I am sure I would not have seen these polyps if I had not used the proctoscope. Proctoscopy is simple and carries very little risk. In the last three months I discovered three polyps which I would have missed except for this maneuver, and I do not encounter a particularly large number of cases of this sort.

I think the suggestion about antibiotics is a very practicable one today.

There was one other point made which I think is very important, and that is that the surgeon ought to be a pathologist, because the pathologists tend to lead us astray very often. They call these polyps cancers on the basis of a few cells which are removed from the periphery.

We consider any polyp to be a killing cancer if there is any induration on palpation or if there is an ulcer in the polyp.

MODIFIED TECHNIQUE FOR TOTAL COLECTOMY IN ULCERATIVE COLITIS

LAURENCE S. FALLIS, M.D.
AND
JAMES BARRON, M.D.
DETROIT

THE MODERN concept of the operative treatment of ulcerative colitis is that when surgical intervention is indicated the objective of the surgeon should be complete colectomy and that ileostomy should be considered only as the first step of a two-stage procedure that will finally result in the extirpation of the entire colon including the rectum. The history of the surgery of ulcerative colitis, as exemplified by the gradually increasing scope of the surgical intervention, is a fascinating story of surgical progress. The first surgical procedures aimed at providing a means of irrigation of the diseased colon with antiseptic solution, but the futility of appendicostomy and cecostomy was soon manifest. Ileostomy alone, in spite of its frequent employment as a last-resort measure, had a much longer vogue. Deflecting the fecal current by ileostomy frequently was a lifesaving measure, but complications arising in the diseased colon, such as acute exacerbation of the disease, arthritis and dermatitis due to toxic absorption, fistula formation, pseudopolyposis, cancer, etc., indicated the necessity for colectomy. Graded resection of the colon soon yielded to complete colectomy, with or without removal of the rectum, though it is now clear that the rectum should be removed in practically every instance, for it is rare for the rectum to be uninvolved. The one-stage operation, with partial colectomy and ileostomy all completed at one sitting, as proposed by Miller, Gardner, and Ripstein,[1] is gaining increasing acceptance as the operation of choice when the general condition of the patient permits.

The removal of the whole colon and rectum, while not the formidable procedure it once was, still is an operation of considerable magnitude. The abdominal part of the operation is usually well tolerated, and problems arising from the fall in blood pressure usually occur during the perineal portion of the operation or immediately after it is concluded. In an endeavor to reduce the extent of the operation, we, following the suggestion of Best,[2] Ravitch,[3] Bacon,[4] Devine,[5] and others, have

From the Department of Surgery, Henry Ford Hospital.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 6, 1953.

1. Miller, G. G.; Gardner, C. McG., and Ripstein, C. B.: Primary Resection of the Colon in Ulcerative Colitis, Canad. M. A. J. **60**:584, 1949.

2. Best, R. R.: Anastomosis of the Ileum to the Lower Part of the Rectum and Anus: Report on Experiences with Ileorectostomy and Ileoproctostomy, with Special Reference to Polyposis, Arch. Surg. **57**:276-285, 1948.

3. Ravitch, M. M.: Anal Ileostomy with Sphincter Preservation in Patients Requiring Total Colectomy for Benign Conditions, Surgery **24**:170-187, 1948.

4. Bacon, H. E., and Trimpi, H. D.: The Selection of an Operative Procedure for Patients with Medically Intractable Ulcerative Colitis, Surg., Gynec. & Obst. **91**:409-420, 1950.

5. Devine, J., and Webb, R.: Resection of Rectal Mucosa, Colectomy, and Anal Ileostomy with Normal Continence, Surg., Gynec. & Obst. **92**:437-442, 1951.

been removing the colon and rectum through an abdominal incision. The colon and rectum are completely mobilized down to the upper surface of the levator ani muscles. The rectum is cut across at this point and removed together with the colon. The perineal portion of the operation is minimal, consisting only of the removal of approximately 1 cm. of anal and rectal mucosa and submucosa.

TECHNIQUE

With the patient under spinal anesthesia when possible, the surgeon, standing on the left side of the patient, makes a long left rectus pars median incision to enter

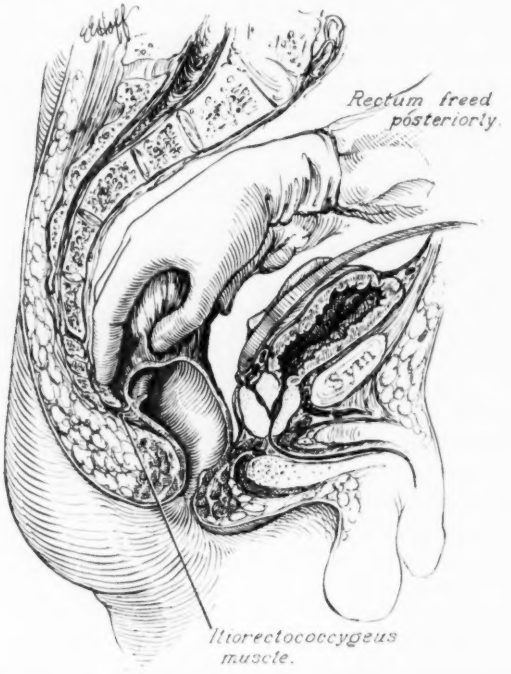

Fig. 1.—Posterior mobilization is carried well beyond the coccyx. Triangular iliorectococcygeus muscle must be sectioned to free the backward curve of the rectum.

the abdominal cavity. The colon is carefully inspected to rule out evidence of cancer. The operation is begun by carefully dissecting the great omentum from the transverse colon. This is easily accomplished if the avascular acquired attachment of the insertion is recognized and utilized for the separation. The presence of a carefully preserved omentum provides a natural covering for the small intestine after colectomy. The stomach with the attached great omentum is then pushed upward out of the operative field. Mobilization of the right colon is more difficult if the patient has had a previous ileostomy, but in either case it can be more easily accomplished by working from above downward by freeing the hepatic flexure first and then gradually working downward to mobilize the cecum and the terminal

ileum. If ileostomy has not been performed previously, section of the ileum is deferred until mobilization of the colon and rectum is complete. Likewise, the splenic flexure is mobilized from below upward after making the initial peritoneal incision in the left colonic gutter close to the ascending colon. Foreshortening of the colon from fibrosis brings both flexures to a lower level than they normally occupy, thereby facilitating mobilization. The peritoneum of both surfaces of the sigmoid mesentery is cut close to the bowel margin so as to fashion peritoneal flaps to be used later in forming the new pelvic floor. The left ureter is identified and

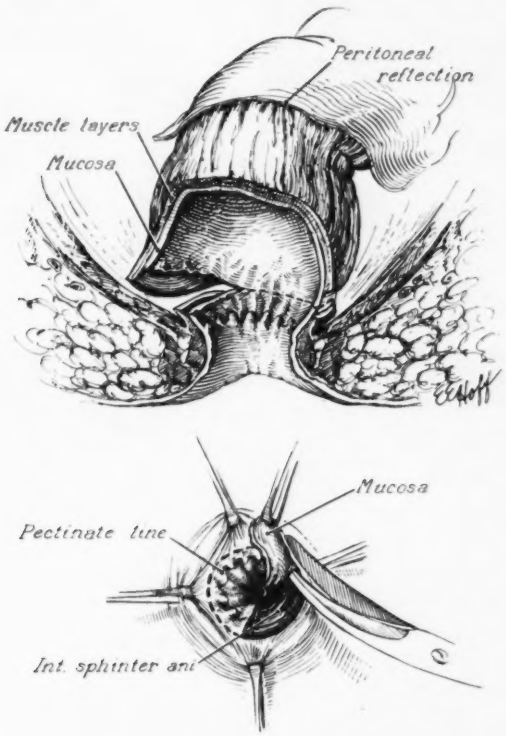

Fig. 2.—With long curved scissors the muscularis and submucosal coats of the rectum are cut close to the attachment of the levatores. Increased upward traction on the completely mobilized bowel allows section of the mucosa just above the dentate line.

protected. The superior hemorrhoidal artery is sectioned and ligated by transfixion at the promontory of the sacrum. The rectum and mesorectal fat are then freed from the sacrum by blunt-finger dissection, carefully peeling the peritoneum from the pelvic walls and margins of the rectum and rectosigmoid before sectioning it. In this manner it is possible to preserve more peritoneum than if this structure is cut, as in the initial steps of the classic abdominoperineal resection. Anteriorly the rectum is separated from the bladder and prostate in the male and from the uterus and vagina in the female down to the superior surface of the levator ani group of muscles. The dissection in the male is more difficult, since it is necessary

to incise the superior rectourethralis muscle at the tip of the prostate. An indwelling urethral catheter, No. 15 French, is essential for protection of the urethra. The lateral rectal stalks are now identified and cut across. The contained middle hemorrhoidal arteries require ligation, since they are usually enlarged in inflammatory lesion of the rectum. The rectum is still attached posteriorly to the coccyx by the triangular iliorectococcygeus muscle (Fig. 1).[6] Section of this structure frees the backward curve of the rectum so that it can be straightened out when

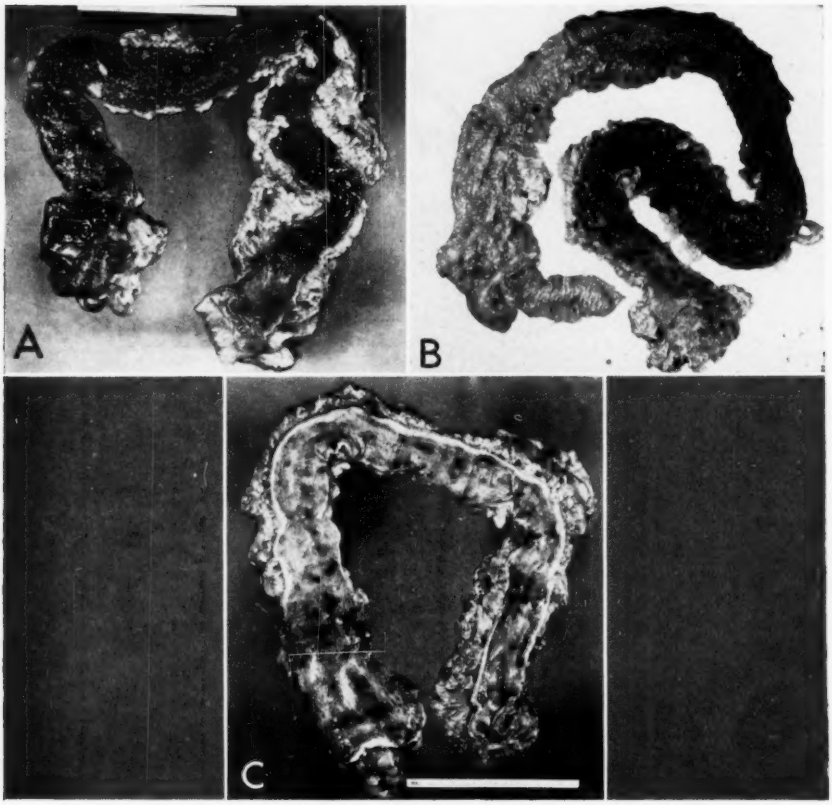

Fig. 3.—*A*, acute ulcerative colitis involving major portion of colon, including rectum. Ileostomy and total colectomy were done in one stage. Staged colectomy would leave area of most advanced disease. *B*, total colectomy was performed six months after ileostomy. Pseudopolyposis was present. *C*, total colectomy was done six months after ileostomy for chronic ulcerative colitis. Note shortening of bowel.

upward tension is applied. The main colonic arterial trunks are cut and ligated by transfixion ligatures. The bowel is removed from the mesentery close to its margin to preserve as much peritoneum as possible. As the right colon is separated from its mesentery, care is taken to protect the right ureter and duodenum. A hernia

6. Courtney, H.: Anatomy of the Pelvic Diaphragm and Anorectal Musculature as Related to Sphincter Preservation in Anorectal Surgery, Am. J. Surg. **79**:155-173, 1950.

tape is now tied around the rectum just above the attachment of the levator ani muscles to minimize soiling. With long curved scissors the muscularis and submucosal coats of the rectum are cut close to the attachment of the levatores. Increased upward traction on the completely mobilized bowel allows section of the mucosa just above the dentate line (Fig. 2). Upon removal of the entire colon and rectum (Fig. 3) the peritoneal floor is repaired. The carefully preserved peritoneal flaps greatly facilitate this closure, and the dependent position assumed by the new peritoneal floor minimizes the area of dead space beneath. After the abdomen is closed, assistants elevate the patient's legs while the surgeon removes the small remaining cuff of mucosa and submucosa (Fig. 2). The operation is completed by inserting two Penrose drains through the anal canal into the space left by removal of the rectum.

COMMENT

This technique has been used in 12 operations as follows: 8 complete colectomies following previous ileostomies; 2 removals of sigmoid and rectum after ileostomy and subtotal colectomy, and 2 one-stage ileostomies and complete colectomies. Noteworthy were the good general condition of the patient at the conclusion of the operation, the rapid convalescence, and the lessened morbidity. Moreover, the psychological benefit of leaving an intact sphincteric mechanism cannot be dismissed as unimportant in the type of patient who suffers from intractable ulcerative colitis. The value of cutting the iliorectococcygeus muscle cannot be overemphasized, since this maneuver frees the backward curve of the rectum and permits removal flush with the upper surface of the levator ani muscles.

SUMMARY AND CONCLUSIONS

The entire colon and rectum above the level of the levatores can be removed through an abdominal incision.

Patients tolerate this procedure better than the combined operation.

Morbidity is lessened and rehabilitation enhanced by this procedure.

DISCUSSION

DR. WILLIAM A. ALTEMEIER, Cincinnati: I should like to reemphasize one of the points very briefly alluded to by Dr. Fallis.

Once irreversible changes have occurred in the colon and ileostomy becomes advisable, the plan of treatment recommended to the patient should be one of planned colectomy, either as a primary procedure or as a secondary procedure after preliminary ileostomy. This will diminish the difficulties in obtaining permission for colectomy later and will decrease the danger of intercurrent malignant degeneration while the patient refuses colectomy in the hope that reanastomosis might be possible.

The operation as outlined by Dr. Fallis might well be considered in the management of acute gangrenous colitis. We have seen six instances of this infection during the past 10 years at the Cincinnati General Hospital. This lesion occurred in both men and women and was associated with diffuse or patchy gangrenous changes in the mucous membrane of the colon, signs of peritonitis, marked elevation of the white blood cell count, fever, and profound shock. In such cases the emergency removal of the entire colon is necessary to save the patient from peritonitis and profound sepsis.

With the operation just described by Dr. Fallis, the entire colon could be removed more simply with a single anterior approach, and I am sure it would be of definite value in attempting to save the patient's life.

I should like to ask Dr. Fallis whether he has considered anal ileostomy as part of his operative procedure, as recommended by Best and Ravitch.

Dr. Louis T. Palumbo, Des Moines, Iowa: I should like to congratulate Dr. Fallis on his excellent presentation and on the description of his technique, which simplifies the perineal portion of total colectomy. I am sure it will aid a great deal in lowering the morbidity and mortality rate.

During the past two and one-half years my colleagues and I have performed a one-stage total colectomy in 10 patients, in 5 for ulcerative colitis and in 5 for polyposis of the colon. A preliminary ileostomy was done on three of those patients; in seven an ileostomy was performed at the time of total colectomy. The morbidity rate was very low, and there was no mortality.

I think we can expect a low mortality and morbidity rate if we are very careful in the preoperative preparation period and in having proper blood replacement during and after surgery. Adequate fluid and electrolyte replacement is particularly important during the postoperative period, specifically in those patients in whom ileostomy is accomplished at the time of total colectomy. These patients have not had the opportunity to adjust to an ileostomy and do lose a great deal of fluid and electrolytes from the ileostomy during the first week. We place special emphasis on the potassium, sodium, and chloride levels in these patients.

[Slide] This is a one-stage total colectomy. This is an ulcerative colitis.

[Slide] This is the lower segment removed at the same time.

[Slide] This slide shows another case of far-advanced ulcerative colitis.

[Slide] Here is a case of polyposis of the colon. This patient has two malignant lesions, one in the ascending and one in the descending colon.

[Slide] The last slide shows the lower segment with polyposis of the colon with cancer.

Dr. C. Morrison Schroeder, Milwaukee: I should like to suggest that the level of amputation can be made a bit higher than Dr. Fallis' diagram suggests.

About two weeks ago, after receiving the abstract of his paper in the program, I had occasion to do an abdominoperineal resection of a residual segment after a previous colectomy for ulcerative colitis, and I intended to follow his plan. In dissecting close to the bowel—as one does in ulcerative colitis, in contrast with the radical operation for cancer—I found myself cutting low in the pelvis, in the lumen of the bowel. Consequently, I decided to cut off the segment at that level. In the perineal part of the operation it was found that about 2½ in. (6.3 cm.) of the mucosa had been left. It was a very simple matter to dissect the residual mucosal segment, following the submucosal plane of cleavage.

Dr. William O. McQuiston, Peoria, Ill.: One of the things that Dr. Fallis brought out very briefly was the fact that he slid the patient down on the table for the perineal portion of the operation.

It is only rarely that an anesthesiologist has an opportunity to talk about one of his pet peeves before a group of surgeons. Certainly, in doing any major abdominal work—in fact, work on any part of the body—changing the position of the patient during anesthesia may result in profound drops in blood pressure, and, if the surgeon can (even though it may be more difficult) complete his surgery without radical changes of the patient's position, it is better for the patient's well-being. If the patient is suddenly flipped from a supine position to a prone position and then turned back again, there may be some shock and even death.

Dr. Owen G. McDonald, Duluth, Minn.: We have performed total colectomy with ileostomy on seven patients, with one death. In six, the operation was done for a complication of ulcerative colitis; in the other, for congenital familial polyposis.

Like Dr. Schroeder, I question the necessity for removal of the entire rectum. With the rectum mobilized below the level of the coccyx, the stump can be easily closed over a right-angle clamp. After division of the sphincter muscle posteriorly, a small rubber tube is left in the stump to provide drainage. Trauma is minimized in this way and the stump can be kept under observation with an anoscope.

Shock need not be a major problem if the segments of the colon are adequately mobilized so as to permit ligation of the major vessels at the site of origin.

Indications for total colectomy were outlined in an excellent review by Dr. Bates, of Detroit, about one year ago. The most difficult decisions arise regarding those patients with severe fulminating ulcerative colitis and those with hemorrhage.

[Slide] This specimen was resected from a 38-year-old man who had symptoms for 20 years. Note the obstructing carcinoma of the transverse colon.

[Slide] This patient required three operations for fistula in ano and multiple dilations of a rectal stricture. The specimen demonstrates, in addition, severe involvement of the colon and strictures of the sigmoid and transverse colon.

[Slide] Here we see marked narrowing and foreshortening, which occur in some patients. Simple ileostomy was followed by a gain in weight from 69 to 123 lb. (31.3 to 55.8 kg.), after which a single-stage colectomy was accomplished without incident.

[Slide] This patient had nine hospital admissions, totaling 440 days, with many operations for rectal abscess and fistulae.

[Slide] Here we failed to recognized a carcinoma of the sigmoid when the patient was first seen, and six weeks later there was complete obstruction. After decompression with a Miller-Abbott tube, we attempted a single-stage colectomy. An appreciable spill of intestinal contents occurred from a gangrenous area above the obstructive carcinoma. The gall bladder was the site of a second primary carcinoma. This patient died on the fifth day as a result of hemorrhage from the gall bladder bed.

Recently, I had to correct an ileal prolapse in a patient on whom I did a resection in the Army in 1943. I should like to ask Dr. Fallis if he has any special method to prevent this complication.

DR. LAURENCE S. FALLIS, Detroit: I wish to thank all those who were kind enough to discuss this presentation.

In reply to Dr. McDonald's question, I do not know of any method that will prevent prolapse of the ileostomy, but there are two steps in the operation which apparently are helpful. One, in fashioning the ileostomy, if the mesenteric margin is faced caudally, I think that there is a little less chance of prolapse. The other point is that it is better to make a stab wound for the ileostomy, carefully cutting out a button of skin, so that healing will be more complete around the skin margins. In our practice it has been done only on a limited number of patients, and therefore I am unable to say that it is the answer. The problem seems to be universal.

In reply to Dr. Altemeier's question—Have we considered the restoration of continuity since we leave an intact sphincteric apparatus?—I think the answer must be as follows: Yes, we have considered it but have not as yet practiced it. One of the advantages of leaving the sphincteric apparatus intact is that it helps the patient psychologically. As you all know, these patients are difficult to handle, and if we remove from them all hope of ever restoring continuity by excision of the external sphincteric apparatus, it sometimes brings them into a state from which it is difficult to get them to recover. At the moment I have one patient who is extremely anxious to have this restoration done, and she is willing to accept all the inherent difficulties and risks. I am therefore tempted to attempt the operation in her case.

One of the discussors was talking about multiple polyposis. I have a little story about a patient with multiple polyposis that rather amused me, and perhaps you would be interested in it too. This is the story of a young woman on whom we did a complete colectomy for multiple polyposis, saving the lower part of the rectum and taking care of the polyps there by fulguration. Subsequently she had two separate operations for removal of malignant polyps in the small intestine. After all this, she deserted her family and ran off with a horse trader, who infected her with all the known venereal diseases. I hadn't seen her for three or four years. Finally one day she came into the office, and I said to her, "Mrs. Henderson, what is worrying you?" I was thinking that she had plenty of worries—she had lost the respect of her neighbors, lost her husband, lost her home, her relatives, all of her colon, two parts of her small intestine, and had been infected with all three venereal diseases. I said, "Mrs. Henderson, what is troubling you?" She said, "I'm getting fat, Doctor, and I want you to do something about it."

TRANSCRANIAL REMOVAL OF INTRAORBITAL TUMORS

J. GRAFTON LOVE, M.D.
AND
HENRY W. DODGE Jr., M.D.
ROCHESTER, MINN.

IN 1945 there were 35 cases of orbital tumors removed transcranially reported from the Mayo Clinic.[1] From January, 1945, until December, 1952, an additional 73 orbital new growths were surgically treated at the clinic by this method. Because of the growing interest and acceptance of the transcranial approach to certain growths of the extraocular portion of the orbit,[2] it seems timely to present data on these more recent cases for consideration by our medical and surgical colleagues.

It is essential to state that progressive asymmetric exophthalmos and failing vision are obviously a primary ophthalmologic proglem, for there are inciting causes other than orbital neoplasms. However, since many intracranial conditions, in addition to orbital neoplasms, may be evidenced by ocular and visual signs, closer cooperation among ophthalmologist, radiologist, and neurosurgeon, and utilization of the cranial orbital approach, may accomplish more satisfactorily that which the diagnostic team strives for and which the patient seeks—the preservation of vision and maintenance of ocular function.

DATA AND MATERIAL

In the analysis of the 73 cases in which the transcranial approach was used for orbital neoplasms between January, 1945, and December, 1952, effort was made to avoid including neoplasms arising in or about the face or maxillary antrums and secondarily invading the orbits. Similarly excluded have been many gliomas, meningiomas, lymphomas, and so forth, which occurred primarily in the cranial fossae with minimal orbital extension. Tumors subjected to anterior removal by the ophthalmic surgeons also have not been considered.

Of the patients on whom operation was performed, 40 were females and 33 were males. The youngest patient was 2 months old, and the oldest, 73 years. The average age of patients was 37 + years. Thirty-seven patients had tumors in the right and 35 in the left orbit. One child had tumors bilaterally. The longest duration of symptoms was 12 years and the shortest 1 week. The universal complaints were progressive asymmetric proptosis and blurred or failing vision. Anamnestic review on these patients has been extremely valuable. It was found that temporization, with increasing proptosis and failing vision, for periods as long as several years, had allowed irreversible damage to the visual apparatus to occur in many cases prior to the patient's seeking competent ophthalmologic advice.

From the Section of Neurologic Surgery, Mayo Clinic.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 7, 1953.

1. Love, J. G., and Benedict, W. L.: Transcranial Removal of Intraorbital Tumors, J. A. M. A. **129**:777-784 (Nov. 17) 1945.

2. Dandy, W. E.: Orbital Tumors: Results Following the Transcranial Operative Attack, New York, Oskar Piest, 1941.

EYE EXAMINATION

The technical examination of the eye is, of course, the strict province of the examining ophthalmologist. However, certain easily seen objective evidences of orbital pressure occurred so repeatedly that their presence might serve to excite the suspicion of the physician who initially sees the patient.

Fig. 1 (Case 1).—Preoperative view to demonstrate blue mass in left eye.

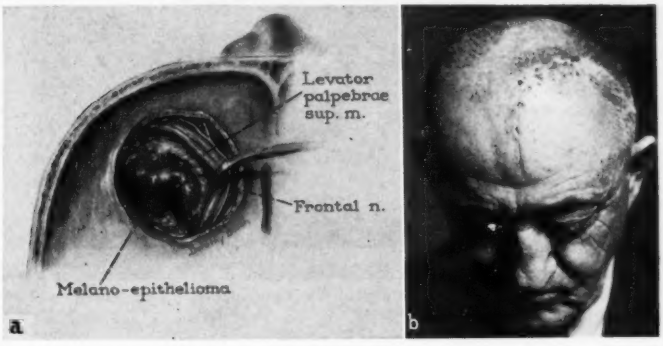

Fig. 2 (Case 1).—(*a*), Appearance at operation of malignant melanoma. (*b*), Appearance of patient in early postoperative phase to show craniotomy incision and receding proptosis of left eye.

Varying degrees of progressive proptosis were common to all patients, and visual loss was common to most. The ocular globe was likely to be deviated from the horizontal and vertical meridians, as judged by pupil position. Limited motion, restricted gaze, and muscle weakness in the affected eye, with the resultant complaint of double vision, occurred frequently.

Pupillary response varied, often remaining normal. The inability of the examiner to displace the globe back into the orbit offered contributory evidence of an increase in intraorbital soft tissue. Frequently, a mass could be palpated. In 12 of our

cases this was true. In one case the tumor could be seen anteriorly (Figs. 1 and 2). Pulsation of the eye, intermittent or constant, and an auscultatory bruit lend added weight to the diagnostician's suspicion.

CASE 1.—A white man, aged 67 years, first registered at the clinic in February, 1949, with the main complaint that his left eye had been becoming increasingly prominent since January, 1948. Anterior exploration of the orbit in August, 1948, had failed to disclose the cause of the difficulty. Recently pain in the left eye was noticeable.

Eye examination showed the vision to be 6/7 and 14/28 on the right and 6/15 on the left. The left eye was markedly proptosed, and motions were restricted in all fields. A blue mass could be seen near the temporal part of the upper fornix. This could be palpated and felt to extend back over the globe. The ocular globe could not be reduced into the orbit by pressure.

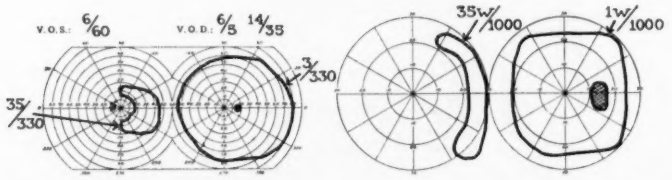

Fig. 3.—Visual-field determination revealed the above pattern in a woman, aged 49 years, whose initial complaints were increasing prominence of the left eye and failing vision, which had been present for 10 years.

Fig. 4.—Operative specimen in same case as in Figure 3 to show meningioma, encountered at operation, which had completely surrounded the optic nerve. This tumor was confined to the extraocular portion of the orbit.

Funduscopic examination revealed the temporal portion of the retina on the left to be elevated 4 D. as compared with the disk, and rough visual fields did not contribute added information. Roentgenograms of the skull and orbits revealed an increased soft-tissue density in the left orbit.

The transcranial approach was recommended, and operation was carried out in March, 1949. A malignant melanoma was identified and removed from the outer quadrant of the orbit. Convalescence was uneventful. Postoperative deep irradiation therapy was given, and the patient was considered for orbital exenteration.

Among the more technical ophthalmologic studies, Hertel exophthalmometry, tonometry, and orbitometry combined with slit-lamp, funduscopic, and visual-field studies frequently aid the experienced ophthalmologist in formulating a working diagnosis (Figs. 3 and 4).

It would seem a worth-while practice to palpate the thyroid gland in all cases and consider a study of basal metabolism in many cases with unilateral progressive exophthalmos accompanied by visual symptoms.

ROENTGENOGRAPHIC EXAMINATION

The careful roentgenographic survey of patients suspected of having an orbital tumor is extremely important. In the new series of cases, 1945 to 1952, there were 44 of 73 patients who showed demonstrable roentgenographic changes (Table 1).

TABLE 1.—*Roentgenographic Changes with Orbital Neoplasms (1945-1952)*

Erosion of bone	Enlargement or erosion of superior orbital fissure or both
Osteomatous thickening of bone	Calcification in orbit
Soft-tissue density in orbit	Thickening of orbital plate
Enlargement or erosion of optic canal or both	Calcification along course of optic nerve
Enlargement or erosion of orbit or both	Orbital phleboliths

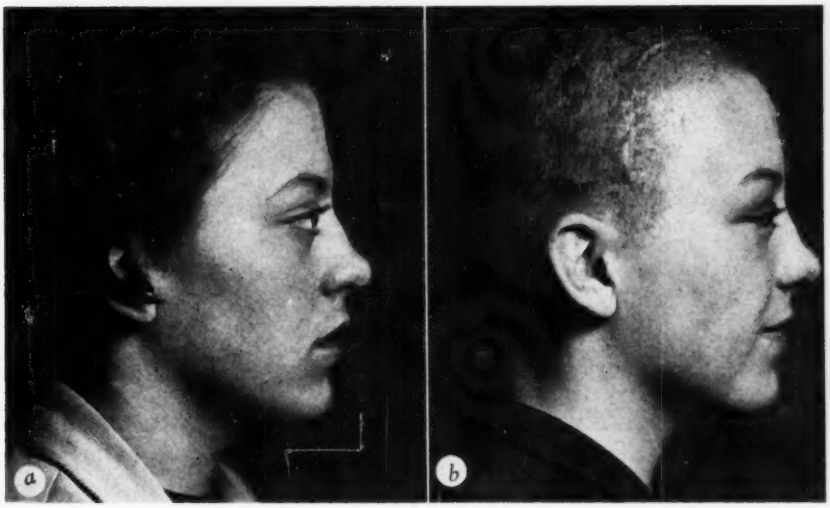

Fig. 5.—(*a*) Preoperative view of patient described in Case 2. (*b*) Same patient on 10th postoperative day.

At the Mayo Clinic, the Section of Roentgenology considers that an adequate study for the orbit might include (1) routine roentgenogram of the skull with stereoscopic lateral views; (2) views of the optic canals; (3) the Caldwell position; (4) the Waters position, and (5) occasionally stereoscopic views of the base of the skull. In a few cases more details of the orbit may be obtained by tomograms. In our opinion, adequate information can be obtained in the large majority by routine views of the skull and optic canals (Figs. 5 and 6).

CASE 2.—An unmarried white woman, aged 18 years, entered the clinic in December, 1951, with the history that one and one-half years previously she had been struck in the face by a basketball. Six months later her right eye began to protrude, and this protrusion became progressive.

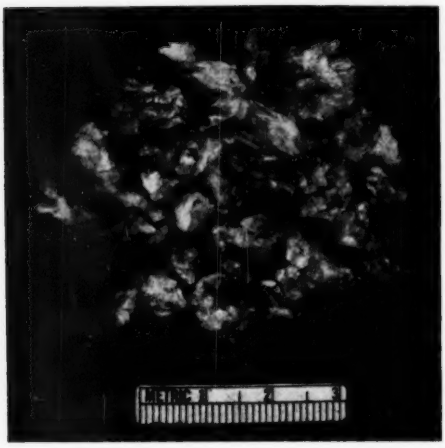

Fig. 6.—Gross specimen of epidermoid tumor removed by transcranial operation in Case 2.

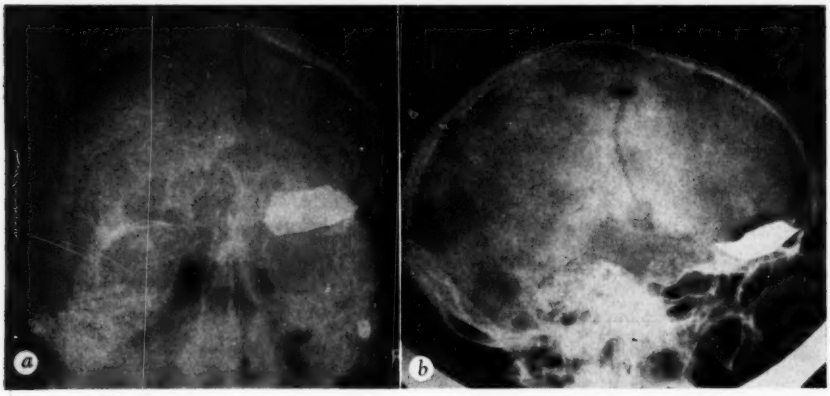

Fig. 7.—Postoperative views of skull to show appearance following stainless-steel orbitoplasty: (*a*) posteroanterior; (*b*) lateral.

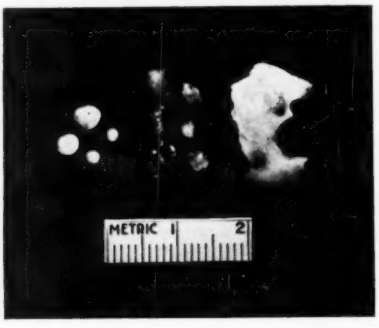

Fig. 8.—Operative specimens in Case 3 to show intraorbital hemangioma and orbital phleboliths.

Eye examination showed the right eye to be prominent, and there were minimal chemosis and scleral injection. The ocular movements and pupillary reaction were normal. Vision in each eye was recorded as normal. Exophthalmometric measurements were recorded at 23 mm. right and 18 mm. left, with a base line of 95. A mass was palpable in the superior temporal quadrant of the proptosed eye. Visual fields were normal, and funduscopic examination showed wrinkling and retinal striations temporally, such as may be encountered with orbital tumors.

Roentgen examination disclosed a defect of bone in the superior and lateral wall of the right orbit, and a soft-tissue mass. A transcranial operation was advised and carried out in December, 1951. At operation an intraorbital epidermoid was removed and a stainless-steel

TABLE 2.—*Intraorbital Tumors Removed by Transcranial Operation (1945-1952)*

	Cases, No.
Meningiomas	19
Intraorbital (8)	
Intraorbital and intracranial (11)	
Hemangiomas	9
Majority cavernous but some mixed capillary and cavernous	
Astrocytomas (gliomas)	5
Pseudotumor (inflammatory?)	5
Metastatic carcinoma	5
Hemangioendothelioma	4
Adenocarcinoma of the lacrimal gland (cylindroma)	3
Neurofibromas	3
Fibrous dysplasia of bone	3
Sarcomas	2
Mixed tumor	2
Lipoid granuloma	1
Fibroma	1
Epidermoid	1
Pyocele	1
Epidermoid carcinoma	1
Malignant melanoma	1
Osteoma	1
Chordoma	1
Hematoma	1
Desmoid	1
Meningoencephalocele	1
Lipoma	1
Unidentified malignant lesion	1
Total	73

orbitoplasty was performed (Fig. 7). The postoperative course was uneventful. An immediately postoperative visual check revealed visual acuity to be 6/10 on the right and 6/7 on the left.

CASE 3.—A white female servant, aged 34 years, was first examined at the clinic in May, 1946, for the complaint of intermittent but slowly increasing prominence of the right eye for 12 years and gradually diminishing vision.

Eye examination revealed the vision on the left to be normal with correction. Exophthalmometer readings were recorded at 23 mm. right and 18 mm. left, with a base line of 102. Complete ptosis of the right upper lid was present, and the patient had previously experienced diplopia. Ocular movement was adequate, and there was no palpable mass. Findings on funduscopic examination and visual fields were unremarkable.

Roentgenograms of the skull and orbits revealed phleboliths in the right orbit. The diagnosis of hemangioma of the right orbit was made, and transcranial operation was advised and carried out in May, 1946.

At operation a cavernous hemangioma was resected from the temporal half of the right orbit and found to contain the phleboliths previously seen in the roentgenograms (Fig. 8). The postoperative convalescence was uneventful. Vision on dismissal was unchanged.

PATHOLOGY

It will be readily appreciated from Table 2 that the gross and microscopic pathologic nature of tumors of the extraocular orbit is amazingly varied in the 73 cases under discussion.[3]

Predominantly these tumors were confined entirely to the orbit (52 cases). In 16 cases there was intracranial extension, and in 5 others adjacent infection, bone proliferation, and congenital defect had played a part.

Although more than half of these tumors are benign growths pathologically if allowed to grow in the narrow confines of the bony orbit, from the standpoint of visual acuity and ocular function in the affected eye, the ultimate outcome for the patient if untreated is malignant—that is, blindness and loss of function.

SURGERY

Final decision as to the surgical treatment for these patients should be based on the considered judgment of a team captained by the ophthalmologist and complemented by the radiologist and the neurosurgeon. The following, in our opinion, are indications favoring the transcranial approach to the orbits:

1. Deep orbital neoplasm (involvement of the orbital apex or superior orbital fissure)
2. Progressive proptosis and visual loss with increasing evidence of circulatory disruption (chemosis, keratopathy) in the absence of metabolic disease, palpable mass, or roentgenographic changes
3. Suspicion or evidence of cranio-orbital or orbitocranial extension
   - (*a*) Involvement of the bone by tumor
   - (*b*) Intermittent or constant pulsatile exophthalmos
   - (*c*) Headache
   - (*d*) Neurologic signs
4. Evidence of a highly vascularized neoplasm
5. Field and nerve-head changes indicative of early encroachment on the optic nerve with minimal pressure signs.
6. Palpable tumor mass anteriorly which the examining team feels may extend too far posteriorly to be removed easily by anterior or lateral approach

The surgical diagnostic armamentarium for further evaluation of orbital lesions includes contrast orbitography with air or mediums (direct injection into Tenon's capsule), percutaneous carotid angiography with 35% iodopyracet (Diodrast), and encephalography. A careful anamnesis and critical clinical examination have proved in our hands, however, to be of distinctly more value than these mechanical aids.

The advantages offered by transcranial approach to the orbits are (1) excellent direct visualization of the orbital contents and extent of lesion; (2) minimal necessity for palpatory exploration (lessened trauma to soft tissue); (3) more adequate control of hemorrhage by means other than pressure; (4) added decompression of orbital contents; (5) opportunity for exploration of optic nerve, optic chiasm, and adjacent brain areas; (6) simultaneous removal of bilateral tumors; (7) utilization

3. Forrest, A. W.: Intraorbital Tumors, Arch. Ophth. **41**:198-232 (Feb.) 1949. Ingalls, R. G., in discussion on Orbital Tumors, Am. J. Ophth. **32**:1595-1596 (Nov.) 1949. Reese, A. B.: Tumors of the Eye, New York, Paul B. Hoeber, Inc., 1951.

of intrahairline incision, which results in little postoperative cosmetic defect, and (8) opportunity for total removal of benign or low-grade malignant tumors.

Apart from the suppurative tumors and far-advanced malignant lesions, neoplasms situated well anterior and certain malignant lesions of the globes (retinoblastoma), which are best handled by the ophthalmic surgeon, the most important contraindication to transcranial orbital surgery is the natural reluctance and apprehension of the patient toward undergoing craniotomy.

In all cases the classic transfrontal or frontotemporal craniotomy with osteoplastic or free bone flap was used. Unless there was specific indication for opening the dura, an extradural approach to the orbit was employed. This aids in reducing the hazard of intracranial complication should an air sinus be inadvertently entered or an inflammatory or malignant lesion encountered. In addition, an intact dura may afford added protection to the frontal lobe of the brain on the operative side.

Surgical hypotension (hexamethonium compounds, and so forth), improved hemostatics, intravenous replacement of blood and fluid, intratracheal combined anesthesia with high oxygen concentrations, the necessity for minimal brain retraction and better visualization of the orbit afforded by an indwelling spinal catheter for withdrawal and replacement of spinal fluid, and increasing familiarity by the neurosurgeon with the local and regional anatomic problems posed by extraocular intraorbital masses have all contributed to minimizing the risk of surgical intervention.

In those cases following removal of an orbital tumor in which the postoperative orbital edema promised not to be excessive, a small stainless-steel orbitoplasty has been performed, covering the decompression in the orbital roof[4] (Fig. 7). This may prevent subsequent pulsation of the globe, which in rare cases has been annoying. The local care of the eye following operation is the province of the ophthalmologist. Blepharorrhaphy has only seldom been necessary.

In cases of orbital malignant lesions, a stainless-steel covering for the orbital roof at the time of transcranial operation will allow the ophthalmic surgeon subsequently to perform orbital exenteration (as for adenocarcinoma of the lacrimal gland) without fear of entering the cranial cavity.

In certain cases in which postoperative orbital edema may be excessive the surgeon may wish to avoid steel cranioplasty but may tack a layer of polyvinyl sponge over the orbital decompression, thus assuring a solid, tough neomembrane of fibrous connective tissue, which may lessen any postoperative tendency toward pulsation.[5]

The defect left by the rare superior orbital encephaloceles or posterior encephaloceles, which is difficult to plate after repair, may be covered by polyvinyl sponge, as was done in a more recent case, not here included (Fig. 9).

CASE 4.—A girl aged 5 months was brought to the clinic in 1952 because the parents thought the right eye had been prominent since birth and was becoming more noticeable.

4. Scott, M., and Wycis, H. T.: Experimental Observations on the Use of Stainless Steel for Cranioplasty: A Comparison with Tantalum, J. Neurosurg. **3**:310-317 (July) 1946.

5. Grindlay, J. H., and Waugh, J. M.: Plastic Sponge Which Acts as a Framework for Living Tissue: Experimental Studies and Preliminary Report of Use to Reinforce Abdominal Aneurysms, A. M. A. Arch. Surg. **63**:288-297 (Sept.) 1951.

Eye examination showed the right eye to be pushed forward and down. There was a palpable mass in the upper temporal quadrant.

Roentgen examination showed the right orbit to be enlarged. Transcranial approach proved the intraorbital mass to be a meningoencephalocele (Fig. 9). This was removed.

Postoperative convalescence was uneventful.

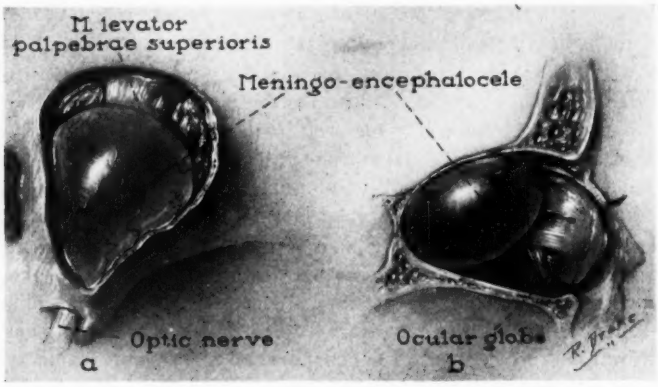

Fig. 9 (Case 4).—Unusual mass encountered in the orbit of a girl aged 5 months. This proved to be a meningoencephalocele: (*a*) from above; (*b*) from side.

Fig. 10.—(*a*) Preoperative view of a housewife, aged 37 years, who underwent transcranial operation and complete removal of a left intraorbital encapsulated hemangioendothelioma. (*b*) Postoperative view taken four months following operation.

More recently, experience in the use of the acrylic resin pentocryl [6] for cranioplasties has suggested that the ease of use, rapidity, molding qualities, durability,

6. Woringer, E.; Schwieg, B.; Brogly, G., and Schneider, J.: Nouvelle technique ultrarapide pour la réfection de brèches osseuses craniennes à la résine acrylique: Advantages de la résine acrylique sur le tantale, Rev. neurol. **85**:527-535 (Dec.) 1951.

and relative inertness of this material may offer a rapid and satisfactory way to cover certain orbits prior to closure of the incision. The radiolucency of this product is an added advantage. In balding men in whom the burr holes from craniotomy may prove unsightly, tantalum, stainless-steel, or acrylic buttons obviate this problem.

There were three postoperative deaths. Two of these occurred in patients with sphenoid-ridge and intraorbital meningiomas. A third patient, with a hemangio-endothelioma of the orbit, died postoperatively of peripheral collapse. Reopening of the craniotomy was required in three cases for evacuation of an extradural blood clot. Frank wound infection occurred in three cases, and two bone flaps became devitalized.

Early removal of benign tumors produced extremely gratifying results (Fig. 10). Eyes that were severely involved by benign tumors or malignant orbital tumors had poorer recovery but in general seemed to have fewer postoperative disabilities directly attributable to operation than might have been expected from other approaches.

Roentgen or radium therapy was employed in 19 cases postoperatively for one or more causes. Orbital exenteration was considered or carried out for seven patients because of malignant orbital involvement.

SUMMARY

Data on 73 orbital neoplasms treated surgically by the transcranial route at the Mayo Clinic between January, 1945, and December, 1952, are presented. Briefly discussed are presenting complaints, objective eye findings which any physician without special ophthalmologic training may recognize, the importance of adequate roentgenograms of the skull and orbits, and the amazingly varied pathologic changes encountered in the extraocular portion of the orbit.

We list our indications for transcranial surgery of the orbit, cite illustrative cases, mention newer aids to safer cranial surgical technique, and recommend stainless-steel, acrylic, or polyvinyl orbital repair in certain types of cases. The advantages, disadvantages, and complication of the transcranial approach to tumors of the orbit are briefly discussed.

CONCLUSIONS

On the basis of the earlier experiences in 35 cases of orbital tumors removed transcranially at the Mayo Clinic, the increased knowledge gained in the review of the 73 orbital neoplasms reported here, and the added experience provided by 28 orbital decompressions for progressive malignant exophthalmos from metabolic disorder performed at the same institution,[7] we believe that transcranial surgery of the orbits for neoplasms is a safe and practicable method. In certain tumors of the extraocular orbit this approach has distinct advantages over other methods, and the denial to the patient of consideration as a candidate for this type of surgery should his lesion be amenable to this approach, is to deny him the fullest chance of attaining the ultimate therapeutic goal—intact vision.

7. Craig, W. M., and Dodge, H. W., Jr.: Surgical Treatment of Progressive Exophthalmos, Ann. Surg. **136**:366-374 (Sept.) 1952.

DISCUSSION

DR. ROBERT C. BASSETT, Ann Arbor, Mich.: I think you have probably just heard presented the largest series of such cases yet recorded.

Our experience with this technique has been limited. However, I do wish to emphasize the point that Dr. Dodge has made, that this is by every means the most ready approach to the orbital contents. The superimposed craniotomy adds approximately 15 or 20 minutes to the operation and allows one full command of the orbit and its contents as well as any intracranial extension of the pathology.

I should like to ask the authors whether or not they have used autogenous bone as well as the acrylics and tantalum mesh in the reconstruction of the orbital roof.

The point that Dr. Dodge made concerning early diagnosis is very important. Many of these persons, as this series shows, have benign lesions. I think it is the experience of all of us that most of the lesions encountered in any series are benign in over half of the cases. For that reason, when these lesions are not treated we have again the tragedy of laissez-faire, of which most unenlightened persons are guilty.

DR. HENRY W. DODGE, JR., Rochester, Minn.: I do not recall that we have used autogenous bone in any of our cases. I think tantalum and stainless-steel were the first repair materials used, and just more recently we have started to use polyvinyl sponge (Ivalon), which Dr. Grindlay and his associates have been using, and, even more recently, acrylic, a very rapid method of performing a cranioplasty. Actually, it takes seven minutes to make the plate, and we have started using that in some cases.

NOCARDIOSIS

Aerobic Actinomycosis with Emphasis on the Alimentary Tract as a Portal of Entry

ROBERT C. HICKEY, M.D.
AND
EARL M. BERGLUND, B.A.
IOWA CITY

NOCARDIOSIS is an actinomycotic infection caused by an aerobic genus of the family Actinomycetaceae. The fungus incriminated most frequently is Nocardia asteroides, and the infectious process may vary from a frank abscess to a granulomatous lesion. The treatment has been disappointing. Many of the published descriptions of the disease have dealt with pulmonary lesions and metastatic intracranial abscesses, most frequently a fatal issue. In this presentation we wish to point to the surgical importance of the disease and to present a relationship to the alimentary tract; data on animal pathogenicity studies, data on antibiotic and chemotherapeutic sensitivity studies, and the importance of an awareness of the disease coupled with the need for energetic therapy are also presented.

CLASSIFICATION

In 1943 Waksman and Henrici [1] devised the currently accepted classification of the family Actinomycetaceae. Prior to this time any discussion of the Actinomycetaceae was hampered by a lack of common terminology. The fungi of human actinomycotic infections are essentially of two biologic types. The anaerobic organisms, of which Actinomyces bovis is the usual infecting agent, cause more disease. A. bovis is a Gram-positive, non-acid-fast, anaerobic or microaerophilic parasite that produces true mycelia characterized by angular branching and irregular fragmentation. In exudates the mycelia are radially arranged, with the periphery often terminating in club-like forms. The aerobic type is exemplified by N. asteroides, and this is the most frequent infecting type. The Nocardia are Gram-positive, non-acid-fast, or acid-fast obligate aerobic saprophytes free-living in nature. They may be filamentous or fragment into bacillary or coccoid forms presenting a variable morphology, which on morphologic grounds alone might resemble Mycobacterium tuberculosis. In exudates macroscopic tangled masses of mycelia may appear with colors ranging from white to yellow to deep red.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 7, 1953.

From the Departments of Surgery and Pathology (Bacteriology), Veterans Administration Hospital, and the Department of General Surgery, State University of Iowa College of Medicine.

1. Waksman, S. A., and Henrici, A. T.: Nomenclature and Classification of the Actinomycetes, J. Bact. **46**:337-341, 1943.

The N. asteroides strains related to the cases reported herein were cultured in a modified Brewer's thioglycollate medium and isolated on 3% human blood agar plates and on Sabouraud's plates at 37 C. and 20 C. aerobic incubation. Confirmatory biochemical studies included the inability of the organism to ferment carbohydrates, to produce indole, to produce hydrogen sulfide (H_2S), to produce ammonia, and to liquefy gelatin.

HISTORICAL

In 1890 Eppinger [2] described the first case of nocardiosis in a human being, a patient who had a metastatic brain abscess at necropsy with concomitant pleuropulmonary disease. The first case in which the disease was primarily intra-abdominal was reported by MacCallum [3] in 1902, and the second instance, by Foulerton [4] in 1910. Both were necropsy studies, MacCallum's case as a consequence of a gastrostomy and Foulerton's, an appendicostomy. Sporadic reports followed, and in 1921, Henrici and Gardner [5] were able to assemble 26 cases and to add their own nonfatal case in which the patient was treated with an autogenous vaccine. In 1952 two reviews [6] appeared in which 40 and 43 cases were collected, and together these reviews added 4 cases with one survival.

Not included in the reviews is an article by Cullen and Sharp,[7] published in 1951, wherein are included two cases of aerobic actinomycosis following external trauma. The fungi were not identified further but were presumably a Nocardia species. One patient was improved and the other cured at the time of publication. In the cases reported, patients survived the nocardiosis; 9 of these cases have been reported since 1944. The specific therapy leading to improved results rests with adequate surgical intervention and the use of antibiotic and chemotherapeutic agents. Apparently Poulton, in 1937, quoted by Dorling and Eckhoff,[8] was the first to use sulfonamide therapy in any form of actinomycosis. He directed a sulfonamide drug against a beta hemolytic Streptococcus associated with an abdominal A. bovis infection and effected a cure of the actinomycosis.

REPORT OF CASES

The following histories are presented. All patients were white men and were hospitalized in the Veterans Administration Hospital, Iowa City. With respect to Nocardia, it is to be noted that in all instances confirmatory culture(s) were

2. Eppinger, H.: Über eine neue pathogene Cladothrix und eine durch sie hervorgerufene Pseudotuberculosis (cladothrichica), Beitr. z. path. Anat. u. z. allg. Path. **9**:287-328, 1890; Wien. Klin. Wchnschr. **3**:321-323, 1890.

3. MacCallum, W. G.: On the Life History of Actinomyces Asteroides, Zentrabl. Bakt. **31**:529-547, 1902.

4. Foulerton, A. G. R.: The Milroy Lectures on Streptotrichoses and Tuberculosis: Lecture II, Lancet **1**:626-631, 1910.

5. Henrici, A. T., and Gardner, E. L.: The Acidfast Actinomycetes with a Report of a Case from Which a New Species Was Isolated, J. Infect. Dis. **28**:232-248, 1921.

6. (*a*) Cruz, P. T., and Clancy, C. F.: Nocardial Osteomyelitis and Septicemia, Am. J. Path. **28**:607-627, 1952. (*b*) Bernstein, I. L.; Cook, J. E.; Plotnick, H., and Tenczar, F. J.: Nocardiosis: 3 Case Reports, Ann. Int. Med. **36**:852-863, 1952.

7. Cullen, C. H., and Sharp, M. E.: Infection of Wounds with Actinomyces, J. Bone & Joint Surg. **33B**:221-227, 1951.

8. Dorling, G. C., and Eckhoff, N. L.: Chemotherapy of Abdominal Actinomycosis, Lancet **2**:707-709, 1940.

obtained, other than in Case 6. Also to be noted is that each patient was followed by examination, other than in Case 6. It is to be understood that the patients received general supportive therapy in addition to specific therapy.

CASE 1.—A 32-year-old filling-station operator entered the hospital on March 12, 1952, complaining of a left upper abdominal sinus of two months' duration. Nearly three months before admission he had noted fatigue and left chest pain on inspiration; later he had chills and fever with periumbilical pain. He was hospitalized elsewhere and given penicillin and another antibiotic. Roentgenograms were said to reveal virus pneumonia. Intravenous pyelograms showed nothing abnormal, and examination of the gastrointestinal tract was noncontributory. The abdominal findings increased, and he became disoriented briefly. Two months before admission 1,500 ml. of pus was released from the left side of the abdomen, and after the drains were removed, at 7 days, purulent drainage persisted.

TABLE 1.—*Composite Data in Cases of Nocardiosis*

Patient	Age, Yr.	Occupation	Disease	Culture	Therapy	Result
1	32	Gasoline station	Pneumonia (?), metastatic intra-abdominal abscess	N. asteroides, hemolytic Staph. aureus	Penicillin, 41 days; sulfadiazine, 19 days; potassium iodide solution, 39 days; drainage	Cured
2	25	Marine Corps	Acute appendicitis, periappendiceal and pelvic abscesses	N. asteroides, beta hemolytic Strep., E. coli, Ps. aeruginosa	Penicillin, 27 days; streptomycin, 5 days; sulfadiazine, 21 days; potassium iodide solution, 21 days; appendectomy; drainages	Cured
3	18	Factory laborer	Branchogenic cyst	N. asteroides	Penicillin, 16 days; extirpation	Cured
4	28	U.S. Army	Pilonidal cyst and sinus	N. asteroides	Penicillin, 12 days; sulfadiazine, 12 days; excision	Cured
5	57	Handyman	Ischiorectal abscess	N. asteroides, Strep. faecalis, nonhemolytic Staph. aureus, E. coli	Penicillin, 5 days; streptomycin, 5 days; oxytetracycline, 16 days; sulfadiazine, 28 days; drainage	Improved
6	41	Invalid	Bronchiectasis emphysema	N. asteroides	None	Incidental finding

The patient was born in Iowa, lived in a small town, and was a farmer prior to 1942. He had been in several southern states and in Australia and the Philippines during World War II.

On examination a tall, ill, febrile, emaciated man was seen who weighed 110 lb. (49.9 kg.). The neurologic examination revealed nothing abnormal. The abdomen was slightly distended, and a mass was palpable adjacent to a left rectus scar, with a purulent sinus. The thick green pus was flecked with tiny reddish granules.

The laboratory data were as follows: The findings on urinalysis were normal. The blood count showed 3,600,000 red blood cells, 11 gm. of hemoglobin per 100 cc., and 8,850 white blood cells. Roentgenograms of the chest revealed nothing abnormal, and roentgenograms of the sinus tract, upon injection with iodized oil, showed extensive ramifying intra-abdominal tracts. Actinomycosis was suspected, and smears showed myriads of mycelia.

The patient's preoperative treatment entailed intensive sulfadiazine and penicillin therapy. On March 17 the sinus tract was exposed, and a loculated, ramifying, granular abscess was evacuated of 1,000 ml. or more of pus; the abscess extended from the left hemidiaphragm along the left gutter to the pelvis. Bleeding was profuse, and 1,500 ml. of blood was replaced.

Postoperative therapy consisted of the administration of procaine penicillin G, 300,000 units twice daily for 41 days; sulfadiazine, 6 gm. daily and later 4 gm. daily for 19 days (stopped because of agranulocytosis), and saturated potassium iodide solution for 39 days, starting with 5 drops, increasing to 15 drops thrice daily, and maintained. The drains were removed after 15 days.

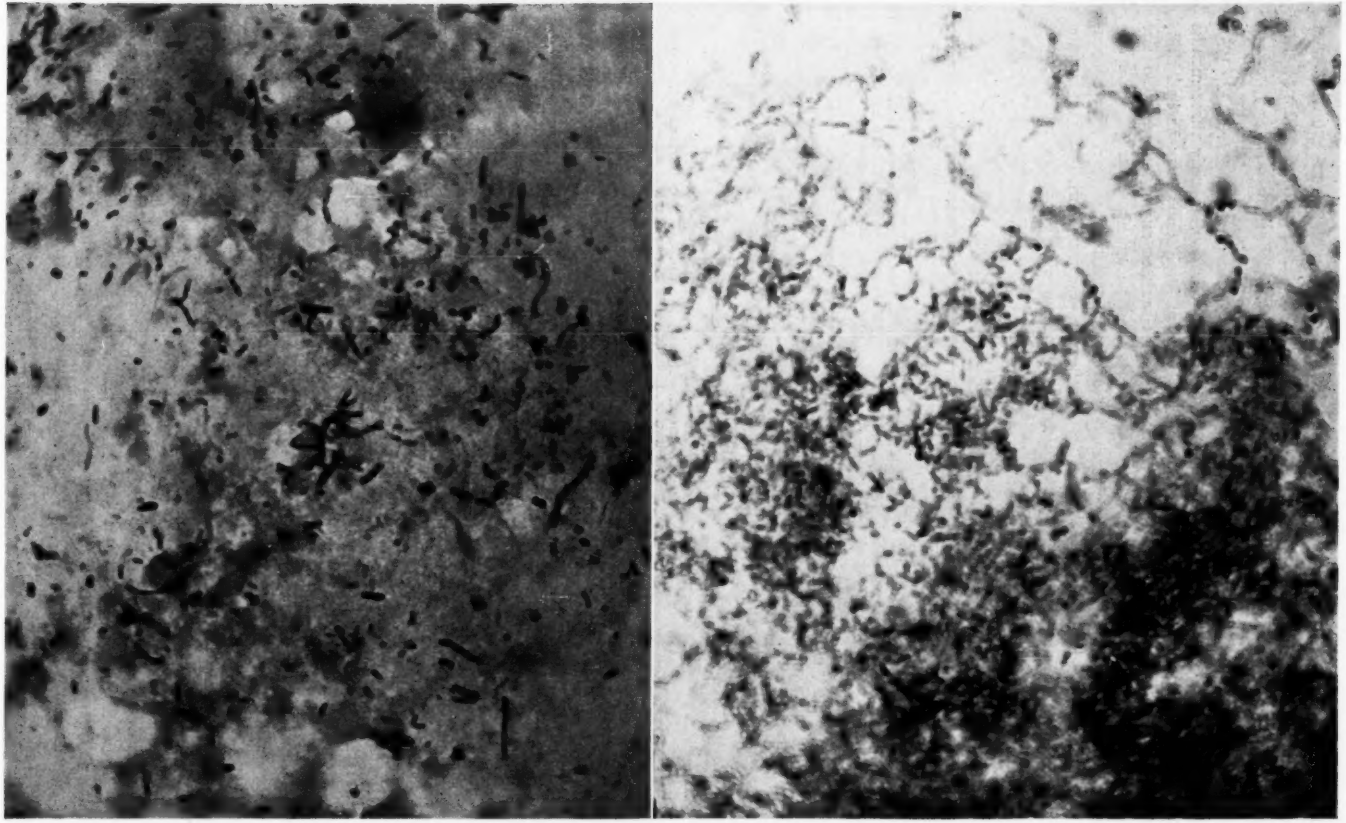

Fig. 1.—Left, photomicrograph of smear of pus taken in Case 2 at operation. Darkly stained Nocardia mycelium shows bacillary and coccoid forms (Gram's stain). Right, photomicrograph of a culture. Tangled clumps of mycelia are seen (acid-fast stain).

The patient became afebrile after the 5th day, and the wound healed by the 40th day. Roentgenographic studies of the intestinal tract showed no abnormalities.

On four occasions, preoperatively and at operation, cultures yielded N. asteroides and hemolytic Staphylococcus aureus. The wound culture yielded no fungi at the 30th day. This patient has been well for six months.

CASE 2.—A 24-year-old Marine Corps officer was admitted on June 18, 1952, because of a six-day illness consistent with acute appendicitis. Penicillin had been administered for three days. Other history revealed that he had been stationed in and about Washington, D. C., during the preceding year and had also lived in Iowa and South Carolina. He had never had a severe respiratory disease.

An acutely ill, febrile man was seen. The abdomen was slightly distended, and demonstrated a right lower quadrant mass with localized peritoneal irritation; there was bogginess and

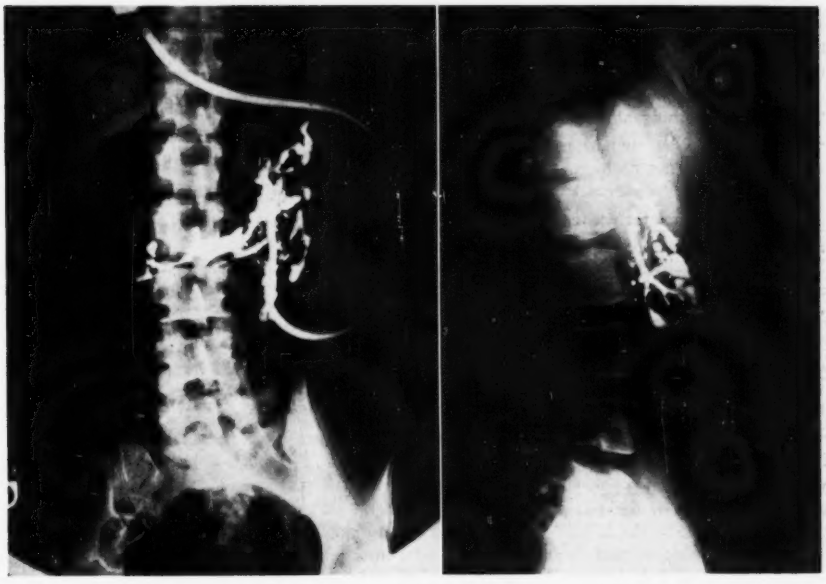

Fig. 2.—Roentgenograms. Iodized oil has been injected into the sinus tract in Case 1. Intra-abdominal ramification of the abscess is noted.

tenderness in the cul-de-sac. The laboratory data revealed normal findings on urinalysis. The white blood cell count was 17,250, with a preponderance of neutrophiles; the red blood cell count, 4,340,000, and hemoglobin, 13 gm. per 100 cc. Roentgenograms of the chest showed nothing abnormal.

That evening the right lower quadrant was explored through a laterally placed incision, and 150 ml. of thick, green, odoriferous pus was released. The pus contained orange granules. A perforated gangrenous appendix was removed without entering the walled-off general peritoneal cavity, and the wound was drained.

Culture of the pus yielded N. asteroides, beta hemolytic Streptococcus, Escherichia coli, and Pseudomonas aeruginosa. The patient was given procaine penicillin G, 400,000 units twice daily, and this dose was continued for 27 days. Streptomycin was also administered, 0.5 gm. twice daily for 5 days; on the sixth postoperative day sulfadiazine was given, 4 gm. daily for 21 days, and also saturated solution of potassium iodide, starting with 5 drops, increasing to 15 drops thrice daily, and maintained. On the eighth postoperative day a pelvic abscess was

evacuated transrectally of 500 ml. of thick green odoriferous pus, which on smear showed actino-like mycelia and grew out N. asteroides and the described bacterial flora. Drains were removed from the abdomen after 14 days and from the rectum after 8 days. The patient became afebrile six days after the rectal drainage. Repeated cultures of the abdominal wound failed to reveal N. asteroides during convalescence.

The patient was discharged to a United States Navy hospital with a tiny right lower quadrant sinus, and further cultures there failed to show Nocardia. He has been well for six months.

CASE 3.—An 18-year-old man was hospitalized on Aug. 9, 1952, with a mass in the right cervical region. The mass appeared first in October, 1951, while he was in Texas, and subsided with penicillin therapy; it reappeared in January, 1952, and in April, 1952, and subsided each time after aspiration by a physician. Six weeks before admission the mass reappeared, enlarged, and became painful.

The patient lived in an Iowa city and had been briefly in Texas. He had never had an oral discharge or foreign taste.

On examination he was febrile (102 F.) but not acutely ill. The patient had trismus, and a firm cystic inflammatory mass measuring approximately 8 by 10 by 8 cm. was located beneath the superficial cervical fascia and anterior to the upper third of the sternocleidomastoid muscle. The faucial tonsillar area was not inflamed, and the remainder of the physical examination revealed nothing abnormal.

Laboratory data showed normal findings on urinalysis. The white blood cell count was 7,700, with 70% neutrophiles, the red blood cell count, 4,100,000, and the hemoglobin, 12 gm. per 100 cc. Roentgenograms of the chest and cervical spine revealed nothing abnormal.

A branchogenic cyst was considered as the clinical diagnosis. The patient was given procaine penicillin G, 300,000 units twice daily. On the first and fourth hospital days the mass was aspirated aseptically of 15 and 12 ml. of thick grey pus, which yielded on each occasion N. asteroides in pure culture; at each aspiration 100,000 units of aqueous penicillin was placed within the mass.

On the 11th hospital day the mass was barely palpable and was totally extirpated. The histologic structure was that of a branchogenic cyst without specific invasive infection. Cultures were omitted. Penicillin therapy was continued for five days (total 16 days), and the patient has been well for a known four months.

CASE 4.—A healthy 28-year-old Army sergeant was seen on Nov. 18, 1952, because of an inflamed pilonidal sinus and a cyst of six weeks' duration. A small abscess adjacent to a sinus was drained, the grey thick pus cultured, and local therapy advised in anticipation of definitive therapy. Culture of the pus yielded hemolytic Staph. aureus and N. asteroides. He entered the hospital three weeks later. The physical examination, laboratory data, and chest roentgenograms were within normal limits. The pilonidal infection appeared quiescent, and the several sinuses had ceased drainage. He had travelled widely in the Far East and in the United States.

Preoperatively and after operation the patient received procaine penicillin G, 300,000 units twice a day, and sulfadiazine, 4 gm. daily for 12 days. On the third hospital day a wide pilonidal cystectomy was done with primary closure. On histologic study no specific changes were noted, but the sinus tissues again grew out hemolytic Staph. aureus and N. asteroides. The wound healed, and the patient has been well for two and one-half months.

CASE 5.—A 57-year-old man was hospitalized on Jan. 21, 1952, because of an ischiorectal abscess of seven days' duration, with associated perineal pain, chills, and fever. He had had an ischiorectal abscess drained with apparent cure at the identical site 16 months previously.

He was a life-long resident of an Iowa city and by occupation did odd jobs.

A bulging large ischiorectal abscess was drained of 400 ml. of yellow foul pus on Jan. 22, and drainage was instituted. At this time the chest roentgenogram and other physical findings were within normal limits. The urinalysis was satisfactory, and the initial blood count showed 15,900 white cells, with 75% neutrophiles; 3,410,000 red blood cells, and 10.5 gm. of hemoglobin per 100 cc.

Procaine penicillin G, 300,000 units twice daily, and streptomycin, 0.5 gm. twice daily, were initiated but were discontinued after five days when the cultures yielded N. asteroides, nonhemo-

lytic Staph. aureus, Streptococcus faecalis and E. coli. The bacteria were not sensitive to penicillin, and consequently oxytetracycline (terramycin), 1.0 gm. daily, and sulfadiazine, 4 gm. daily, were given for 16 days and 28 days, respectively. In the early postoperative phase, a repeat culture yielded N. asteroides and the same bacterial flora. The wound healed slowly, and it is too early for a final opinion.

CASE 6.—A 44-year-old patient was hospitalized for 39 days because of pulmonary invalidism with severe emphysema and bronchiectasis. The history and physical findings were consistent with these diseases. He had not worked for six years; he had been a farmer. Cultures on routine sputum study yielded N. asteroides.

SENSITIVITY STUDIES

The N. asteroides strains, as indicated in Table 2, were tested against various concentrations of penicillin, chloramphenicol, chlortetracycline (aureomycin), oxytetracycline, streptomycin, sulfamerazine, and sulfadiazine in thioglycollate broth. Although it is recognized that in vitro performance may not be paralleled by human in vivo effectiveness, when possible, these tests should be carried out. The fungi

TABLE 2.—*Drug Sensitivity of Nocardial Strains, in Micrograms per Milliliter of Thioglycollate Medium*

	Case 1		Case 2		Case 3		Case 4		Case 5		Case 6	
	G*	I†	G	I	G	I	G	I	G	I	G	I
Sulfadiazine	..	5	5	10	..	5	5	10	10	50	5	10
Sulfamerazine	10	50	5	50	10	50	10	50	10	50	5	10
Oxytetracycline	..	1	1	3	1	3	3	10	1	3	1	3
Streptomycin	10	100	3	10	3	10	10	100	10	100	10	100
Chlortetracycline	1	3	10	100	1	3	3	10	3	10	1	3
Penicillin	..	1	..	1	1	3	..	1	..	1	..	1
Chloramphenicol	3	10	..	1	3	10	3	10	1	3	3	10

* G, growth.
† I, inhibited.

were inhibited by broth concentrations of sulfadiazine at levels less than the blood concentrations [9] obtained, except in Case 5. Penicillin inhibited growth well, as did oxytetracycline. It must be stated, however, that in animal protection studies compared with sensitivity studies, Runyon [10] noted incomplete correlation; this latter finding was noted by him particularly with use of chlortetracycline.

After removal of the organisms from the concentrations of drugs which inhibited growth, those fungi previously in contact with sulfadiazine or sulfamerazine grew on reinoculation. The antibiotics appeared to have caused death of the Nocardia.

PATHOGENICITY STUDIES

Further animal pathogenicity studies are in progress, and only preliminary observations may be reported. Adult Swiss mice were available as the experimental animals. The organism for animal inoculation was grown in thioglycollate broth.

Eight mice were inoculated with a 10-day old culture of Strain II (Case 2), four intraperitoneally with 0.25 ml. and four intracranially with 0.05 ml. of inocu-

9. Free sulfadiazine.

10. Runyon, E. H.: Nocardia Asteroides: Studies of Its Pathogenicity and Drug Sensitivities, J. Lab. & Clin. Med. **37**:713-720, 1951.

lum. At 72 hours the animals were killed. Control animals similarly treated showed no detectable changes. The Nocardia was recovered from the particular cavity injected in each experimental animal. Of those injected intracranially, the brain was softened grossly, and, microscopically, small necrotic areas with peripheral lymphocytic infiltration were noted. Scattered tiny white nodules, which grew out Nocardia, were seen on the peritoneal surfaces in animals inoculated intraperitoneally. Two mice from this group showed pulmonary abscesses; although culture of the lungs yielded N. asteroides, the possibility of experimental contamination may not be overlooked.

In another study 72-hour cultures of Nocardia from each patient were used. Eight mice were used for each strain, and the inocula consisted of 0.05 ml. delivered intracranially into each of four mice and 0.25 ml. of inoculum and 0.25 ml. of sterile gastric mucin [11] delivered intraperitoneally into each of four mice. Control injections of gastric mucin were innocuous. There was a marked variation in pathogenicity. Within 48 hours the organism in Case 5 proved fatal to seven of eight animals; that in Case 6 to one injected intraperitoneally, and that in Case 4 to one inoculated intraperitoneally. The organisms were recovered on culture as described previously. The findings were those of encephalomalacia and mild peritonitis, the latter of which showed viscous fluid macroscopically. The remaining viable animals, while apparently ill for 72 hours, are being observed further.

COMMENT

The clinical syndrome of nocardiosis must be highly variable and modified by host resistance, pathogenicity, and duration of disease. Much of the reported data deal with necropsy studies in cases in which the disease was of long standing and disseminated hematogenous metastases the rule. Primary pulmonary infections are prevalent, but external trauma can allow the disease to involve soft tissue and bone. The course of the patient may be that following an emaciating illness, with local and blood-borne spread of the infection. The Nocardia have probably no true invasive power. Through an epithelial disruption, a nidus of infection becomes established, and the clinical train of events pursue a course to death unless interrupted by fortuitous or therapeutic events. The distribution of the cases as shown by Cruz and Clancy [6a] indicates a world-wide dispersion; also, our small series offered no geographic trend or urban or rural prevalence.

The Nocardia are saprophytes free in nature, and Gordon and Hagan [12] isolated and studied pathogenic and nonpathogenic aerobic actinomyces from soil. One must accept therefore the fact that the Nocardia are widely prevalent. We believe that in Case 6 the fungus was an incidental finding and unrelated to any pathologic process. The saprophytic organism was present, having gained access by inhalation or ingestion. Eckhardt and Pilcher [13] presented a case of nocardiosis in which a tooth was extracted and a chronic brain abscess ensued, becoming symptomatic

11. Strauss, R. E., and Kligman, A. M.: The Use of Gastric Mucin to Lower Resistance of Laboratory Animals to Systemic Fungus Infections, J. Infect. Dis. **88**:151-155, 1951.

12. Gordon, R. E., and Hagan, W. A.: A Study of Some Acid-Fast Actinomyces from Soil with Special Reference to Pathogenicity for Animals, J. Infect. Dis. **59**:200-206, 1936.

13. Eckhardt, K., and Pilcher, J.: Brain Abscess Due to Nocardia Asteroides, Texas J. Med. **46**:915-919, 1950.

two months after the extraction, and for which surgical intervention was unsuccessful one and one-half years later. The extraction site healed. Tucker and Hirsch [14] reported a case of cervical nocardiosis, the onset of which was antedated four months by a tooth extraction. In Case 3, demonstrating the branchogenic cyst, it might be postulated that the fungus entered the cyst through the tonsillar area; it appears less tenable that the organism was introduced in the distant past at the time of aspiration by physicians. The case of the Marine Corps officer with a perforated gangrenous appendicitis (Case 2) offers conclusive evidence that the organism gained access to the infected spaces via the bowel (appendix) perforation. The colon bacterial flora associated in this infection would further support this, even were the appendiceal perforation not seen. It might be added that the appendix showed no nidus of actinomycosis in its coats on pathologic examination, thus tending to support the contention that the invasion must be initiated by other than the Nocardia. Binford and Lane [15] reported a fatal case of disseminated nocardiosis in which the patient's initial symptoms accompanied grippe and an ischiorectal abscess. It is difficult to tell in which anatomic site the infection commenced. One cannot refute that it might have been pulmonary, but certainly it is equally tenable to incriminate the ischiorectal space, for, in addition to the fatal brain abscess, N. asteroides grew out from both sites at death. In Case 5, that of the patient with the ischiorectal nocardiosis, there was no other area of known involvement. Thus the infection appeared to be primary. The intact exposed perineum and the associated bacterial flora point to contamination of the ischiorectal space by colon contents, secondary to intestinal leakage.

The site of primary infection in Case 1 is unknown. The patient presented himself with a draining left abdominal abscess and the Staphylococcus or the Nocardia could have been individually either the primary agent or a contaminant from the exterior. With a Staphylococcus it is most unusual to have a single hematogenous intra-abdominal large abscess with a healed primary, but with nocardiosis such is frequent. Therefore credence might be placed on the pneumonia reported elsewhere, which cleared with antibiotics, and the abscess drained and treated by us represented a metastatic N. asteroides abscess. It appears plausible that the pilonidal nocardial infection (Case 4) resulted from external invasion along the sinus tracts from surface contamination.

It becomes difficult to refute that the Nocardia saprophyte may infect through a defect in the alimentary tract. It appears most logical that the postoperative peritonitis observed by MacCallum and Foulerton in patients, one of whom had a gastrostomy and the other an appendicostomy, resulted from intestinal spillage of Nocardia and not from introduction of the organism from the exterior. Cuttino and McCabe [16] in their study on N. intracellularis allude to an intestinal-tract origin of the disease without conclusive proof. The mechanism of infection thus approaches that seen with an anaerobic A. bovis; the Nocardia may infect through routes of inhalation, skin penetration, or ingestion.

14. Tucker, F. C., and Hirsch, E. F.: Nocardiosis, with a Report of 3 Cases of Actinomycosis Due to Nocardia Asteroides, J. Infect. Dis. **85**:72-86, 1949.

15. Binford, C. H., and Lane, J. D.: Actinomycosis Due to Nocardia Asteroides: Report of a Case, Am. J. Clin. Path. **15**:17-23, 1945.

16. Cuttino, J. T., and McCabe, A. M.: Pure Granulomatous Nocardiosis: A New Fungus Disease Distinguished by Intracellular Parasitism, Am. J. Path. **25**:1-48, 1949.

The therapeutic results obtained appear quite satisfactory. It is acknowledged that all patients were healthy adult males, other than in Case 1, in which the patient was severely debilitated and in Case 6, in which the finding of N. asteroides was incidental. We were fortunate, too, in having no metastatic brain abscess. Prior to any therapy, recognition of a disease must be forthcoming and the poor results with nocardiosis in the past occurred generally as a consequence of long-standing illness. Therefore an awareness of aerobic actinomycosis is essential to surgeons who are called upon to treat infections. In the light of our present knowledge, the chemotherapeutic agent of choice is sulfadiazine in appropriate dosage coupled with an antibiotic, of which penicillin and oxytetracycline have proved effective. The potassium iodide saturated solution may or may not offer additional benefit. Adequate free surgical drainage or extirpation of the nocardiosis is imperative. All therapy must be early and vigorous, and supportive measures must not be neglected.

SUMMARY

Nocardiosis, an aerobic actinomycotic infection, is an infrequent but poorly recognized disease. These saprophytes demonstrate variable pathogenicity and gain access to infection through an epithelial disruption through routes of skin penetration, inhalation, or ingestion. Once an infection is established the prognosis may be ominous. Appropriate surgical intervention (wide drainage or excision), chemotherapy (sulfadiazine), and an appropriate antibiotic (penicillin or oxytetracycline) have proved effective in therapy. A series of five cases of nocardiosis with survival are presented.

The criticism and opinions of Dr. J. R. Porter, Professor of Bacteriology, State University of Iowa College of Medicine, were most helpful.

DISCUSSION

Dr. William A. Altemeier, Cincinnati: This is a very interesting paper, and it emphasizes several points.

In the past we have tended to discount the aerobic types of actinomyces as being pathogenic and capable of producing clinical types of actinomycosis. However, in the past few years, these organisms have assumed increasing importance, and evidence is accumulating that clinical actinomycosis can be caused by either aerobic or anaerobic strains.

We agree with Dr. Hickey that its is possible for these organisms to produce infection by way of the alimentary tract. It is frequently possible to culture both the aerobic and anaerobic types of actinomycetes from the oral cavity in perfectly normal subjects. In fact, examination of tonsils removed during tonsillectomy will often show the actinomycetes in the crypts of the tonsils without evidence of surrounding inflammation. From this source the organisms may penetrate the tissues of the buccal cavity through breaks in the mucous membrane, as was demonstrated by Dr. Hickey, may be aspirated to produce pulmonary infections, or may be ingested to produce abdominal types of actinomycosis.

Occasionally we have seen human bite infections of the hand caused by aerobic strains. This slide indicates a patient with actinomycosis of the finger produced by one of the aerobic species. There was an associated destruction of the cartilage and joint and a particularly destructive osteomyelitis.

In our limited experience, the two types of actinomycosis, produced by the aerobic and anaerobic organisms, resemble each other.

During the past 13 years we have encountered 24 cases of actinomycosis. In 21, the anaerobic Actinomyces bovis was the etiologic agent, and in 3, only aerobic species were isolated. The other two cases of the aerobic variety were an intra-abdominal abscess secondary to a ruptured appendix and a pneumonitis which was confused for six months with tuberculosis.

I was particularly interested in Dr. Hickey's conclusion that sulfadiazine, used in conjunction with penicillin or oxytetracycline (terramycin), was the chemotherapeutic agent of choice for nocardiosis. We would agree in this, but we believe penicillin is the primary agent to be used in full dosage for approximately three to four months in the cases that are well established. Sulfadiazine, used in conjunction with the penicillin, is given in doses of 1 gm. every six hours, daily for three weeks. Thereafter, smaller doses are administered for periods up to a year and a half, depending upon the extent and nature of the lesion.

In patients who are sensitive to penicillin or who have infections produced by strains resistant to penicillin, oxytetracycline may be used with sulfadiazine.

Here is a group of slides that illustrate the importance of prolonged chemotherapy with both penicillin and sulfadiazine or sulfamerazine. This patient had actinomycosis of the thorax and thoracic wall which replaced the lung. It involved the mediastinal structures and produced a fistulous tract between the trachea, the esophagus, and the axilla. There was also erosion and bisection of the clavicle, producing the deformity visible on the slide. Treatment with penicillin and sulfadiazine produced considerable improvement in three weeks, and one and one-half years later, all evidence of active infection had disappeared. This picture was taken in 1943, and the patient has remained well up to the present.

DR. ROBERT C. HICKEY, Iowa City: With respect to therapy, I do not believe that Dr. Altemeier and our group are at variance. We use penicillin in full therapeutic doses, but in the particular cases presented, we do not feel that it was necessary to continue it as long as he indicated.

None of our patients was as severely ill as the one Dr. Altemeier described.

We feel that the sulfadiazine is very, very important, and if we were not using sulfadiazine, we would use sulfamerazine. In the one patient for whom the sulfadiazine course was particularly short, an agranulocytosis developed, and thereupon we discontinued its use.

I wish to thank Dr. Altemeier for his discussion.

MALIGNANT TUMORS OF THE SOFT TISSUES OF THE EXTREMITIES

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THE THERAPEUTIC management of malignant soft-tissue tumors of the extremities may be simple and uncomplicated but also may become a most difficult and perplexing situation, particularly when the tumor has approached the border line of curability by metastasizing to the regional lymph nodes. There seems to be no unanimity of opinion as to the ideal therapeutic methods that should be utilized when such a situation is encountered. This is in distinct contrast to the uniformity of thought on the management of the primary tumor as well as the associated lymph-node-bearing area in certain other regions of the body. Treatment of carcinoma of the breast, for example, until recent years at least, was a generally accepted, uniform surgical exercise, as was also the treatment of carcinomas in various locations of the large intestine, with the possible exception of the rectum. The standardization of extensive surgical procedures for the management of cancer in these locations may have been fostered by the fact that such operations do not produce disfigurement that is readily apparent. On the contrary, the removal of a large mass of tissue for a malignant tumor of an extremity yields notable anatomical and functional impairment.

A conspicuous example of the complexity of the problem in an extremity is the epidermoid carcinoma, which is a relatively simple neoplasm to treat when it is small and has not metastasized but which challenges the ingenuity of the therapist when it has extended to such lymph-node-bearing areas as the axilla or inguinal region. The extremes of thinking with respect to the management of these regions are exemplified, on the one hand, by Johnson and Ackerman,[1] who state that prophylactic axillary dissections in carcinoma of the hand are not indicated when the cancer lies above the sweat gland level, and, on the other, by Frieden [2] and also by Taylor, Nathanson, and Shaw,[3] who state, in effect, that prophylactic dissection of the regional lymph nodes should be performed. Interscapulothoracic amputation and hemipelvectomy have not received significant consideration for this situation.

From the Departments of Surgery and Pathology, Indiana University Medical Center.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 7, 1953.

1. Johnson, R. E., and Ackerman, L. V.: Epidermoid Carcinoma of the Hand, Cancer **3**:657-666, 1950.

2. Frieden, J. H.: The Regional Lymph Node Dissection in Cancer of the Extremities, Surg., Gynec. & Obst. **89**:591-598, 1949.

3. Taylor, G. W.; Nathanson, I. T., and Shaw, D. T.: Epidermoid Carcinoma of the Extremities with Reference to Lymph Node Involvement, Ann Surg. **113**:268-275, 1941.

With the hope of clarifying some of these issues, particularly those concerned with treatment of regional nodes, all cases of all patients with malignant neoplasms of the extremities, with the exception of those arising in bone and accessory bone structures, referred to the Indiana University Medical Center for treatment of either the primary or a recurrent tumor prior to July 1, 1952, have been analyzed, espe-

TABLE 1.—*Pathological Classification*

Type of Lesion	Patients, No.
Epidermoid carcinoma	67
Fibrosarcoma	23
Basal cell carcinoma	7
Malignant melanoma	7
Rhabdomyosarcoma	5
Liposarcoma	2
Miscellaneous	5
Total	116

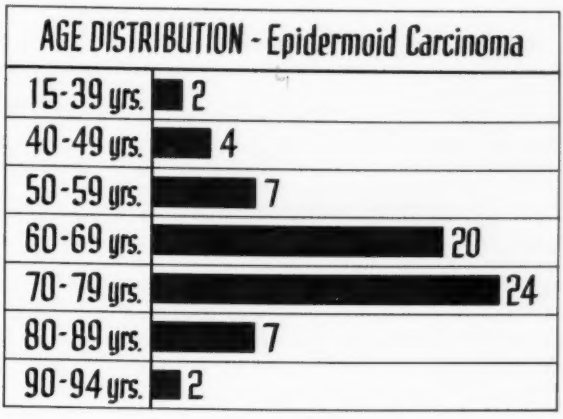

TABLE 2.—*Pathological Grade*

Epidermoid Carcinoma	No.
Well differentiated	31 (46%)
Moderately differentiated	22 (33%)
Poorly differentiated	12 (18%)
Undifferentiated	2 (3%)

cially from the point of view of therapeutic results. All have been pathologically verified, and all pathological material has been reviewed by one of us (F. V.) without prior knowledge of the therapeutic results achieved. The pathological classification is presented in Table 1.

CARCINOMA

Squamous Cell Carcinoma.—There were 67 patients, 55 males and 12 females. The age distribution of the 66 patients whose ages were recorded is presented in the Chart, which emphasizes the preponderance of this particular neoplasm in the

seventh and eighth decades of life. The mean age was 67.5 years. The pathological grading is illustrated in Table 2. As has been mentioned by others, the growth potential of these neoplasms, as estimated by the grading, tends toward the well-differentiated types.

The five-year period of survival after the initial therapy was used as the criterion of successful control of the tumor. The three-year span, as proposed by some, is inadequate. Four of our patients died with cancer between the third and the fifth year after the primary treatment. Nine of the 67 patients (Table 3) were treated for less than five years prior to July 1, 1952, and have been excluded, although all but one are living. No patient was lost to follow-up. The study group consisted of 58 patients. Twenty-five, or 43%, of the 58 survived five years. In analyzing the success or failure of therapeutic methods, we established two groups of patients, one consisting of the 25 patients who lived five years or more and who therefore were considered successfully treated, and the second consisting of 18 patients who died in less than five years with known cancer and whose treatment was considered a failure. The 15 patients who died in less than five years without cancer are excluded from this comparative analysis.

TABLE 3.—*Epidermoid Carcinomas*

No. of patients		67
Treated less than 5 years	9	
Lost to follow-up	0	
Patients available for study		58
Survived for 5 yr. or more		25 (43%)
Survived less than 5 yr.	33	
Died with cancer	18	
Died without cancer	15	

There were four distinct categories in which there seemed to be significant differences between the patients for whom therapy was a failure and the patients for whom it was a success. These were the location as well as the size of the primary tumor, the pathological grade, and the presence or absence of regional lymph node metastases (Table 4).

Although there was a distinct difference in the location of the tumor in the two groups, with a greater proportion of the tumors in the upper extremity in the therapeutic failure group than was true in the successful group, the number of patients was so small that probably this difference was not of statistical significance. Nevertheless, this contrasts with other reports,[4] which indicate that at least when regional lymph nodes are involved, such as the axillary or inguinal, the prognosis is more favorable in cases of carcinoma of the upper extremity.

As would have been anticipated, the small tumors were prognostically more favorable than the large. Our data on microscopic material were insufficient to permit us to estimate the influence on prognosis of depth of invasion of the neoplasm, as illustrated by Johnson and Ackerman, who stated that in their series metastases did not occur when the tumor had not invaded below the sweat glands. The relation of pathological grade to prognosis was in accordance with what would have been expected. There were only 2 patients in the total group of 67 who had undifferen-

4. Clarke, H. M.: Primary Carcinoma of the Extremity, Surg., Gynec. & Obst. **79**:669-672, 1944. Taylor, Nathanson, and Shaw.[3]

tiated carcinomas, and neither survived. Of the 12 who had poorly differentiated neoplasms, 5 could not be analyzed, and 7 fell into the failure-success groups. Three were unsuccessfully treated and four successfully managed.

The most significant prognostic index was the presence or absence of lymph node metastasis. It was present on admission or developed later in 17, or 25%, of the 67 patients. This was a considerably higher rate than has been recorded by other authors, who have presented rates of 14 to 16%.[5] No patient who had lymph node involvement at the time of admission survived five years, and only two of those in whom that complication developed later were saved for a comparable

TABLE 4.—*Therapeutic Successes and Failures According to Categories*

Category	Therapeutic Failures	Therapeutic Successes
Number of patients	18	25
Location of primary tumor		
Upper extremities	14 (78%)	17 (68%)
Lower extremities	4 (22%)	8 (32%)
Size of primary tumor		
Less than 7.5 cm.[2]	8 (44%)	19 (76%)
7.5 cm.[2] and larger	10 (56%)	6 (24%)
Pathological grade		
Well differentiated	4 (22%)	14 (56%)
Moderately differentiated	9 (50%)	7 (28%)
Poorly differentiated	3 (17%)	4 (16%)
Undifferentiated	2 (11%)	0 (0%)
Lymph node metastasis		
Present on admission	9	0
Developed later	6	2
Indeterminate	3	2
None at any time	0	21
Treatment		
Primary tumor		
Excision	6	16
Radiation therapy	4	1
Amputation	6	7
Miscellaneous	2	1
Metastatic tumor		
Radical dissection of nodes	6	1
Radical amputation	1	0
Radiation therapy	4	1
Excision of node	0	2
No treatment	7	21

period of time. A possible explanation for this high rate of metastasis and poor success in the management of this complication was the fact that several patients had had their original treatment elsewhere and were referred to this center for treatment of recurrences, either locally or in regional nodes.

Therapy and the results from it also are outlined in Table 4. Treatment was mixed in several instances. For example, some patients had both x-ray therapy and excision. However, only the major effective therapy was tabulated. Five of the six amputations in the failure group were of the conservative type, and the other was an interscapulothoracic procedure designed to remove the primary tumor as well

5. Schrek, R.: Cutaneous Cancer: III. Statistical Analysis with Respect to Site, Sex and Preexisting Scars, Arch. Path. **31**:434-448, 1941. Johnson and Ackerman.[1] Taylor, Nathanson, and Shaw.[3]

as the axillary metastases. The primary tumor was not controlled in eight cases of the failure group. In two cases the treatment was local excision; in four, x-ray therapy; in one, a combination of excision and x-ray therapy, and in one, conservative amputation. Four of the primary tumors that were controlled in the therapeutic failure group were treated with conservative amputation, three with local excision, one with electrocautery, and one by radical amputation. One patient refused treatment.

Radical dissection of regional lymph nodes failed to control the metastatic tumor in five of the six cases in which it was performed in the failure group. Furthermore, in two of the six, biopsies of the regional nodes had been done several months prior to the regional dissections and had not shown metastatic tumor. Radical dissection of the nodes was followed by an interscapulothoracic amputation in two patients because of this failure to control the deposits. The axillary recurrence was controlled by this procedure in one of the two, but not in the other. Radical dissection was combined with x-ray therapy in one other instance. In one patient in the success group, with a primary tumor on the middle finger, a nodule developed in the epitrochlear region three years later. This nodule was excised and was found to contain metastatic carcinoma. The area was treated on several subsequent occasions by x-radiation. Eight years after amputation of the primary tumor, the patient died of a pulmonary embolus, and postmortem examination, although it revealed tumor invading the humerus, causing a pathological fracture, showed no other carcinoma in the body. Another similar patient in this group had a digit amputated; three months later an epitrochlear lymph node that was positive for carcinoma was excised. No additional therapy has been done for this patient; yet, strangely enough, he remains alive and well nine years after removal of the neoplasm. Prophylactic node dissection and radiation therapy each were done in one instance in the success group in which tumor in the regional area was never proved.

It was known that two of the patients who died with cancer had distant bone metastases at the time of death.

Basal Cell Carcinoma.—There were seven patients in this group, three women and four men, varying in age from 45 to 83 years. All were treated by wide local excision. Four of the seven survived five years without recurrence. One is living and well two and one-half years after treatment, and two patients died less than five years after therapy for other causes, each without evidence of residual tumor. Thus none of the seven died with cancer.

SARCOMA

Fibrosarcoma.—There were 23 patients with fibrosarcoma, 11 females and 10 males. Their ages were distributed in every decade of life, from the first to the eighth, inclusive. Four of these tumors occurred on an upper extremity and 19 on a lower. Eight were 30 sq. cm. or less in area, and 13 were larger. The size in two patients was not recorded. Seventeen patients died with the disease less than five years after the initial therapy; one patient was lost to follow-up, and five patients survived longer than five years. Four of the survivors were treated with nothing other than wide, but local, excision. One was treated first with an excision, and, when the tumor recurred locally, with a conservative amputation. In another case, a tumor on the ankle is illustrative of the slow growth of some of the fibrosarcomas. The

patient refused treatment for two years. He finally accepted it, but two and one-half years after amputation metastases occurred in the lumbar vertebral bodies, and he eventually died, nearly eight years after the tumor appeared.

Rhabdomyosarcoma.—There were five patients with this tumor, three males and two females. One patient was 7 years of age, and the others were between 64 and 74. Three of the lesions were located on a lower extremity and two on an upper extremity. Two patients were treated by amputation, and each died with tumor four years later. Two had no treatment because of the great extent of the disease at the time they were seen, and these persons lived only a few months. One patient with a tumor on a wrist has survived for six years after the initial therapy. Seven separate excisions of recurrent tumor were performed in a five-year period after its origin, and then another recurrence developed in the forearm. This tumor was excised but recurred quickly, and an interscapulothoracic amputation was performed. Next there developed a metastasis to the soft tissues of the leg, which was removed. It is anticipated that this patient will die of metastatic tumor in the near future.

Liposarcoma.—Only two patients had liposarcoma. One, with a tumor on the thigh, died within eight months after the diagnosis was established. He received x-ray therapy only. The other case, that of a patient with a tumor on the forearm, was another interesting example of the slow yet inexorable growth of sarcomatous malignant tumors. In a 10-year period he had had eight excisions of the tumor, but he died ultimately of generalized metastases, 11 years after the onset of the neoplasm.

MISCELLANEOUS TUMORS

Malignant Melanoma.—This group also was small, consisting of only seven patients, four men and three women, varying in age from 32 to 78 years. Six of the seven tumors were located on the lower extremity, and one on the forearm. One patient refused treatment. The local tumor was excised in all others. An inguinal dissection was done a year after the primary treatment of a melanoma on the leg in one patient because of metastasis to these nodes. This patient has remained well for 18 years and another patient for 6 years, the latter with no treatment except for excision of a melanoma of the heel and radiation therapy to this area and to the inguinal lymph nodes, to which tumor had metastasized. The other patients have died with the disease.

Other Tumors.—There were two patients with reticulum cell sarcoma and one with a hemangiopericytoma, one with a malignant mesenchymoma, and one with a neuroblastoma. All lesions were on the lower extremity, and all patients died within 16 months after the onset of the neoplasm. The patient with a mesenchymoma of the thigh had a disarticulation of the hip, but local recurrences and generalized metastases occurred shortly thereafter.

COMMENT

This report is not an analysis of a planned therapeutic approach for the control of malignant tumors of the soft tissues of the extremities but a factual account of results obtained in a mixed series of patients, with the hope that clearer concepts of therapy can be achieved. Many of these patients had their initial therapy before coming to this institution, and many forms of treatment, in the hands of different surgeons and radiologists, were administered. Some problems were most complex when first encountered, while others were simple.

A squamous cell carcinoma of the skin of an extremity should be an example of the simple, easily controllable tumor. Wide surgical excision seems to be the appropriate therapy, but one must remember that in doing wide local excision or radiation therapy in the few instances in which it may be indicated, the tumor extends in depth as well as laterally and the therapeutic tool should be utilized in such a way as to remove a margin of normal tissue deep to the tumor as adequately as on its lateral borders.

It is the occasions when these neoplasms have metastasized to regional lymph nodes, specifically to the axillary or inguinal groups, that the therapy becomes more complicated and the prognosis ever so much more grave. We suspect that our lack of understanding of the potentials of a tumor to metastasize and our failure to establish definitive, universally accepted therapeutic procedures for this complication, as we have established for carcinomas in certain other areas, are important contributing factors to such failures. It has been mentioned that so-called prophylactic dissections of these regions have been advocated by some. This is an ill-advised, poorly utilized phrase. If defined precisely, it would mean that such operations were being proposed to prevent or to protect the axillary or inguinal regions from being involved with carcinoma. However, in practice, such a phrase probably implies the employment of extensive dissections with the hope that tumor in subclinically evident stages can thus be removed. It has been advocated also that a certain interval of time—some say two weeks, others longer—should elapse between the treatment of the primary tumor and such treatment of regional metastases. Yet, because of our lack of knowledge of the rates of movements of migrating malignant cells through lymphatics, the numbers that are migrating and the routes that they are choosing to take, we have no guide to help us determine a suitable interval. We have, however, a vain hope that these migrating cells will abide by our wishes, and that at the time we choose to do a radical regional lymph node dissection, they will all have conveniently gathered together in a family in these regional nodes, leaving none of their associates behind in the affected limb and allowing none to move onward to higher and deeper lymphatic vessels.

An example of the fallacy of this thinking is illustrated by one of our own patients who was admitted to the hospital recently with an extensive carcinoma of the skin of the knee and metastases to the inguinal lymph nodes, as proved by biopsy. A midthigh amputation was done and, 17 days later, radical iliac, inguinal, and femoral node dissection, carried inferiorly nearly to the point of amputation. A node reappeared in the inguinal operative area two and one-half months later, and the patient was then subjected to a hemipelvectomy. This patient, as well as the two others in whom biopsy of the axillary lymph nodes were negative and in whom proved axillary metastases developed later, serves to emphasize our lack of understanding of the movement of malignant cells from the primary area to the regional lymphatic drainage basins.

Equally unsound, in our opinion, are the operations proposed for resections in continuity of primary tumors, such as malignant melanomas and their local lymphatic deposits. These procedures are designed also with the hope that migrating cells will abide by man-made regulations and will travel through only those subcutaneous and fascial lymphatics that are to be removed in continuity and will not pursue more devious courses to the lymph nodes or move by blood vessels.

When a patient presents himself with a primary extremity carcinoma and proved metastases in the axillary or inguinal regions, is it not sound logic to assume that this tumor has occupied the extremity and has taken possession of it for its own purposes? And should we not conclude that a hemipelvectomy or an interscapulothoracic amputation is a better therapeutic procedure for the removal of the total disease than is isolated therapy to the physically separated but biologically associated manifestations of the process? Grimes and Bell [6] have stated: "It is a long established fact that the smaller the diseased part the easier is the decision to sacrifice it. The larger the part to be excised the greater is the tendency to delay its removal because of the effect upon the individual." This statement is illustrated by our own material in the failure-success groups. There were five tumors that originated on a finger, and all the tumors were amputated. Twenty-three tumors were located on a hand or wrist, but only four were amputated. One was located on a foot, and amputation was performed. Three of the seven tumors located on a leg were amputated. Only one patient, a patient with advanced disease, had a planned interscapulothoracic amputation as a definitive procedure for treatment of the primary and metastatic tumor, and he died with cancer. One might add the thought that quarterectomies are probably used only as measures of desperation, rather than as planned definitive procedures for the removal of an extremity and its lymph node area, similar to the removal of a breast and its lymph node area that has been occupied by cancer.

It is our firm belief that a quarterectomy should be used with greater frequency when metastatic tumor exists. Although widespread metastases do occur from squamous cell carcinoma of the skin, they are not common, and, if they have not occurred at the time the patient seeks treatment, it seems reasonable to us to expect better results from this planned procedure than heretofore have been obtained. The contrast with the practical aspects, however, is very real. It is not easy for a patient to accept, nor for a surgeon to offer, such an operation. This was exemplified, in our hands, recently when two patients, each with carcinoma of the skin of the hand of an extensive degree, were on the service together. One had axillary metastases. He readily accepted an interscapulothoracic amputation. The other was so fearful of any kind of an amputation that it was difficult to keep him in the institution even for excision of the primary tumor and grafting. One might also question the philosophy of advising patients in this age group, with such a short natural life expectancy, to accept this procedure. Although the word mutilation has been used to describe such measures, we have not seen the type of mutilation from this kind of surgery that can be accomplished by a rapidly growing carcinoma.

The situation with sarcomas is different. They are ever so much more unpredictable, pursuing both the vascular and the lymphatic route of travel, and we suspect that because of the inherent, innate, unpredictable growth potential of these neoplasms wide local excision (to the point of amputation if necessary to obtain a wide margin) is just as effective as are the more radical procedures. Of the group of 23 fibrosarcoma patients who survived for five years, reported on by Ivins, Dockerty, and Ghormley,[7] only 4 had amputations, and only 1 of the 4 underwent amputation

6. Grimes, O. F., and Bell, H. G.: Shoulder Girdle Amputation, Surg., Gynec. & Obst. **91**:201-209, 1950.

7. Ivins, J. C.; Dockerty, M. B., and Ghormley, R. K.: Fibrosarcoma of the Soft Tissues of the Extremities: Review of 78 Cases, Surgery **28**:495-508, 1950.

as a primary procedure. Of their 40 patients, one-half that died with the tumors had had amputations, but only four of these amputations were done as a primary procedure. Of these 40 patients, 18 had from one to nine local excisions, emphasizing to a significant degree the great potential of these neoplasms to recur locally and the truly wide local excision that must be utilized if they are to be controlled.

SUMMARY

A series of 116 patients with carcinoma and soft-tissue sarcomas of the extremities is presented.

The serious prognosis when squamous cell carcinoma metastasizes to regional lymph nodes is emphasized.

Interscapulothoracic amputation or hemipelvectomy is suggested as a sounder therapeutic tool for management of the coexisting primary and proved metastatic tumor than isolated therapy to each area.

Because of its varied growth potential and unpredictable routes of metastases, wide local excision is probably as effective as amputation for the treatment of the fibrosarcomas.

DISCUSSION

Dr. Eugene M. Bricker, St. Louis: Aside from the tumors which, because of their size, location, and extent, may require hemipelvectomy or shoulder-girdle amputation for removal, I think Dr. Lawrence has come nearer to a logical explanation of when and why we should advise this radical type of procedure than anyone I know.

I certainly am unable to make a similar statement regarding the arguments advanced for radical amputations in the treatment of melanoma, which is much more unpredictable in its mode of spread than is epidermoid carcinoma of the skin. It is quite understandable that quarterectomies have been used as measures of desperation in the past, and this is likely to continue until more information of the type supplied by Dr. Lawrence is available.

We should all survey our own experiences to see if failures of regional lymph node dissection for epidermoid carcinoma of the extremities justifies a more radical approach. Whether or not a more radical approach will add appreciably to the survival rate will then have to be determined by further time and observation, and there is some question that this result will be achieved with this lesion, as well as with malignant melanoma.

I think it is very possible that quarterectomy will eventually be found to have definite indications which have not been recognized in the past. It seems probable to me that these indications may depend upon such factors as the size and fixation of primary metastatic lymph nodes or of failure with recurrence after so-called "prophylactic dissections."

If Dr. Lawrence would be so kind, I should appreciate a little clarification from him regarding his attitude toward prophylactic dissections now, in light of his recent studies.

Dr. Lawrence is to be congratulated on his clear presentation of the problem. I personally feel greatly stimulated by his presentation, but I am not entirely convinced of the advisability of quarterectomy for epidermoid carcinoma of the extremities with regional metastasis.

Dr. Louis T. Palumbo, Des Moines, Iowa: I should like to confine my remarks to rhabdomyosarcoma. This is a rather rare tumor, and when one is confronted with such a problem and attempts to assess the literature, one finds oneself in a state of total confusion as to how to proceed in the management of such a case. In the past few years we have encountered a few such cases.

I believe that if the lesion is localized to the extremity in an area where it is movable, if it has not invaded the bone, and if there is no evidence of distant metastasis and no invasion of the neurovascular bundle, a very wide excision, including the skin and superficial structures and the muscle groups, may be a satisfactory procedure.

If the lesion is higher and is fixed to bone or to the neurovascular bundles, then a more radical procedure may be necessary, such as high amputation, hemipelvectomy, or forequarter amputation.

I believe the responsibility lies with the physician who sees the patient the first time. Usually the lesion is not expected to be malignant and the local excision is very limited, and the lesion frequently recurs.

[Slide] This patient came to us four and one-half years ago. He is now aged 52. He had a history of a rapidly growing tumor in the anterior upper aspect of the thigh, of a year's duration. We did thorough studies, with repeated aspiration biopsies. You can see the puncture wounds in the skin for the removal of tissue from the tumor. The diagnosis was established preoperatively as a rhabdomyosarcoma.

There was no evidence of bony invasion, and no evidence of distant metastasis. The lesion was not fixed to the underlying structures.

[Slide] A very wide excision was accomplished, removing the skin and superficial structures and practically all of the quadriceps femoris group of muscles and portions of the abductor group, with no evidence of invasion of the vascular sheath. The regional nodes were removed. This is the specimen itself. The excess tissues have been removed from the specimen.

[Slide] This is the immediate postoperative picture, showing the extent of the excision. The patient has a good functional limb. We have followed him now for four and one-half years. There is no evidence of local recurrence or distant metastasis.

[Slide] The next patient came to us last July—a man 38 years of age who gave a history of having a rapidly growing tumor on the upper aspect of the right thigh. He had a local excision about two years ago. In nine months there was rapid recurrence in the same area. A second surgeon in his home community attempted a secondary removal, which again was not wide.

He came to us, asking for hemipelvectomy. At the time of admission he had a very large local recurrence, which was fixed to the underlying structure and showed invasion into the femur; the lesion extended up almost to the pubis. There was no evidence of distant metastasis.

[Slide] A hemipelvectomy was accomplished. This is the specimen.

[Slide] And this is the gross specimen, showing invasion of the femur, as you can see, in the right lower corner.

[Slide] This is the stump about 10 days after operation.

[Slide] And this slide shows the patient, about two weeks later. This patient was called in every three months, and six months later multiple lung metastasis was revealed.

I believe if adequate wide excision had been accomplished at the time of primary surgery his chances for survival would have been greater.

DR. EDWIN A. LAWRENCE, Indianapolis: I want to think Dr. Bricker and Dr. Palumbo for their interesting comments, particularly for the use of the word "desperation," with which I heartily agree.

I honestly believe that some of the disapproval that has been expressed toward the extensive removal of one or another quarter developed because the procedure has been used too late, and that is not the time to use it.

I think Dr. Bricker's question about prophylactic dissection may have been initiated by the report by Drs. Johnson and Ackerman on its use in carcinoma of the hand. They point out that lymph node metastasis does not occur when the tumor has not invaded below the level of the sweat glands.

Our pathological material is too scanty for a similar study. The idea of doing prophylactic dissection raises an interesting question because of the uncertain involvement of the axilla or inguinal region; if, later on, the pathologist finds tumor in the nodes, then it is no longer a prophylactic dissection but a therapeutic procedure.

I do not think we can tell when cells are going to enter those lymph nodes. I think we can do a prophylactic dissection, find nothing in them, and actually have tumor in the process of migrating from the primary site to the lymphatic area. I have done the procedures but must honestly say that I am swinging away from feeling that they are important. I think that if a tumor is not there, we have accomplished nothing. If the tumor is there, I wonder if it is the best operation.

SPLENIC PUNCTURE

DEWARD O. FERRIS, M.D.
AND
MALCOLM M. HARGRAVES, M.D.
ROCHESTER, MINN.

SPLENOMEGALY presents a problem to internist and surgeon alike, and many times more information is needed than is made available by our usual methods of examination. Careful clinical evaluation, examination of the peripheral blood, and study of the bone marrow often leave us without an accurate explanation for the enlargement of the spleen. For this reason, splenic puncture has long been considered a procedure which might be helpful in the differential diagnosis of the splenomegalies. Splenic puncture, however, is not without danger, and the numerous deaths recorded in the past which have followed this procedure have made most workers fearful of employing it. It seemed to us that there still is considerable danger in any splenic-puncture technique in which a piece of splenic tissue is removed for histologic examination. On the other hand, we feel that there is little, if any, danger in the type of puncture which yields material for cytologic study. The major disadvantage, then, in the procedure which we are presenting is that its value is in direct proportion to the ability of the examiner to recognize cytologic changes in the material obtained and to interpret these findings correctly.

The literature of splenic puncture is well covered by both Moeschlin,[1] and Block and Jacobson.[2] Moeschlin's monograph on the subject was translated into English in 1951, and this together with a personal visit to our laboratory in the same year stimulated us to employ splenic punctures again as an aid in the diagnosis of hematologic conditions encountered by us at the Mayo Clinic. Our present observations are based on our experience with 46 splenic punctures done since that time.

SELECTION OF PATIENTS

In the selection of patients for splenic puncture the following essentials must be kept in mind: 1. Only definitely palpable spleens should be punctured. 2. No patients with any hemorrhagic tendency should be subjected to splenic puncture.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 7, 1953.

From the Division of Surgery (Dr. Ferris), and the Division of Medicine (Dr. Hargraves), Mayo Clinic.

1. Moeschlin, S.: Spleen Puncture, translated (from German) by A. Piney, London, William Heinemann, Ltd., 1951.

2. Block, M., and Jacobson, L. O.: Splenic Puncture, J. A. M. A. **142**:641-647 (March 4) 1950.

3. Puncture should not be performed in the presence of a septic splenomegaly or in the instance of a painful spleen, whether owing to stretching of the capsule or to infarction. 4. Unconscious patients and children must never undergo puncture.

TECHNIQUE

In doing our splenic punctures we employ the technique described by Moeschlin. The relative safety of this procedure primarily depends upon two factors, namely,

Fig. 1.—Equipment used in performing splenic puncture.

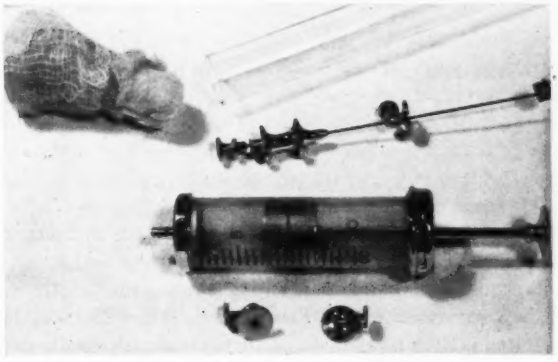

Fig. 2.—Type of syringe, needle, and guard used in splenic puncture.

puncture with a small-caliber needle and immobilization of the spleen by full inspiration. Internal hemorrhage, of course, is the great hazard of splenic puncture and may follow tearing at the splenic capsule or making a large puncture wound in the spleen.

The equipment we use is shown in Figures 1 and 2. The needle employed for the procedure is an ordinary spinal puncture needle which has been equipped with a guard to regulate the depth to which it can be thrust.

Before proceeding with the puncture, one must know the exact location of the spleen, especially its position during full inspiration. The reason for this is chiefly that in this position one avoids the possibility of a quick intake of breath, with the consequent sudden reflex descent of the diaphragm and also the spleen. If the puncture needle were in place, one would almost certainly cause a laceration of the spleen, with perhaps serious bleeding as a result.

With the patient lying on his back, the site of puncture is in the 9th or 10th intercostal space, either in the midaxillary line or slightly anterior or posterior, according to the position and size of the spleen. The position of the spleen (Fig. 3) shows that puncture through the 9th or 10th interspace during full inspiration will avoid adjacent organs.

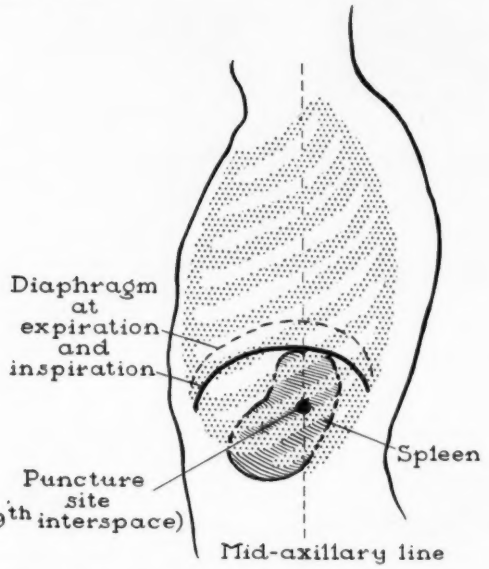

Fig. 3.—Diagram showing position of spleen and site of puncture.

The skin at the site of puncture is carefully cleansed, disinfected, and draped with sterile towels. A 1% solution of procaine hydrochloride is used to anesthetize the skin, subcutaneous tissue, and muscle. One can usually determine when the needle reaches the peritoneum by the patient's reaction. The depth to which the needle has penetrated is then measured and its equivalent, plus about 2 cm., is used as the guide in setting the guard on the puncture needle. This setting permits a penetration of 2 cm. into the spleen and is a safeguard against damage to the large vessels which lie deep in the spleen.

After the guard is set on the splenic-puncture needle, the needle is introduced through the infiltrated area down to the peritoneum. The stylet is now removed, and the syringe is attached to the puncture needle. The patient is told to take a deep breath and then to close his mouth and pinch his nose between the fingers and thumb of the right hand. This maneuver prevents the possible reflex intake of breath at the time of puncture, a reflex which would cause sudden descent of the

diaphragm and spleen with laceration of the capsule by the penetrating needle held rigid in the body wall. As soon as the guard prevents further penetration, one aspirates quickly but strongly once or twice, maintaining suction for several seconds to mobilize splenic elements. Before the needle, together with the attached syringe, is withdrawn, it is essential to release the negative pressure in the syringe by permitting the plunger to go back slowly. If this is not done, negative pressure may explode the aspirated material in the needle back into the syringe as the needle is withdrawn, and the specimen is lost. If the puncture is performed properly, no aspirated material enters the syringe; it remains in the puncture needle.

The material obtained in the needle is tranferred to a small paraffin paper boat and, with a round-tipped glass rod, it is transferred in proper-sized drops to chemically clean glass slides and smeared as are routine blood and bone marrow materials. Staining is the same as for blood or bone marrow preparations. It should be pointed out that speed in handling the material is essential, since splenic pulp material coagulates very rapidly.

If insufficient material is obtained, further puncture may be necessary at the same sitting, and occasionally additional material may be obtained by a second puncture for bacteriologic investigation.

After splenic puncture the patient is kept in bed for six hours as a precaution against hemorrhage.

OBSERVATIONS

We undertook this study to see whether the procedure is a safe one and to see whether it is helpful. In regard to the first objective, we have encountered no difficulty in our series of 46 cases. In this connection, Moeschlin has done more than 300 punctures without a death and essentially without any morbidity. This, together with our experience and that of others employing a similar technique, suggests that splenic puncture can be a relatively safe diagnostic procedure.

We have attempted to show in the Table the value of splenic puncture as a diagnostic aid. The conditions listed were diagnosed on the basis of clinical and hematologic observations. It is evident that in 15 of the 46 cases (32.6%) an accurate diagnosis was made only when the findings contributed by splenic puncture were added to the rest of the clinical and laboratory findings. In an additional 14 cases (30.4%) the splenic puncture confirmed the clinical diagnosis. In five cases (10.9%) the procedure was helpful in a negative way in that it excluded other pathologic conditions, such as Gaucher's or other storage diseases. Splenic puncture appears therefore to be a diagnostic aid in about three-fourths of the cases studied, and would seem therefore to be definitely worth while. Morrison and his co-workers [3] have expressed the same opinion.

The first 10 cases in the Table represent an interesting group in which the marrow has failed, or is failing, and hematopoiesis is being transferred to the spleen. One is not able to make this diagnosis accurately without splenic puncture unless one resorts to exploration or necropsy. In the former, one would have to remove a biopsy specimen from the spleen and await study of the material by a pathologist. In such circumstances one would be dangerously near doing a splenectomy, a

3. Morrison, M.; Samwick, A. A.; Rubinstein, J.; Morrison, H., and Loewe, L.: Splenic Aspiration: Clinical and Hematological Considerations Based on Observations in 105 Cases, J. A. M. A. **146**:1575-1580 (Aug. 25) 1951.

procedure which might be very detrimental to the patient. We believe therefore that this type of condition is the one in which splenic puncture has its greatest value.

It was probably fortuitous that there were four cases of lymphoma in which splenic puncture was diagnostic. In this condition it is a matter of differentiating between pathologic and physiologic immaturity of the reticular and lymphoid elements, and this is admittedly difficult. On occasion, cytologic changes of obvious pathologic significance are seen, for example, a typical Reed-Sternberg cell in a case of Hodgkin's disease.

The case in which "splenic puncture" gave diagnostic evidence of carcinoma of the adrenal gland represents what will happen to all who attempt splenic puncture, that is, mistaking a tumor in the left upper quadrant for the spleen when it is not. In this case a large carcinoma of the left adrenal was mistaken for an enlarged spleen, but the cells obtained by the puncture technique were sufficient to establish the correct diagnosis, confirmed later at surgical exploration of the lesion.

Splenic Puncture as a Diagnostic Aid

	Splenic Puncture, Cases				
Disease	Total	Diagnostic	Confirmatory	Exclusive	No Help
Myeloid fibrosis with myeloid metaplasia of spleen	10	10	..	..	..
Lymphoma	20	4	9	2	5
Chronic myelogenous leukemia	5	..	5	..	..
Granuloma	2	..	..	..	2
Multiple myeloma	1	..	..	..	1
Infectious splenomegaly	1	..	..	1	..
Congestive splenomegaly	1	..	..	1	..
Reactive splenomegaly	1	..	..	1	..
Leucopenia	1	..	..	..	1
Aplastic anemia	1	..	..	..	1
Carcinoma of adrenal gland	1	1	..	..	..
Lupus erythematosus	1	..	..	..	1
Indeterminate	1	..	..	..	1
Total	46	15	14	5	12

In the nine cases of lymphoma and in five cases of chronic myelogenous leukemia in which confirmatory evidence was obtained, the diagnosis was already established with reasonable accuracy prior to splenic puncture. In the two cases of lymphoma listed in the column headed "Exclusive," we were able to exclude other conditions, such as Gaucher's disease and myeloid metaplasia of the spleen. In the other three cases listed in this column we also excluded the likelihood of lymphoma.

COMMENT

Splenic puncture is an important aid to the diagnosis of certain hematologic conditions. It may well prove to be even more helpful in the future if the material obtained can be studied by means of the phase microscope (as suggested by Moeschlin for the differentiation of lymphosarcoma cells).

It is generally accepted that splenectomy is contraindicated if the bone marrow is inadequate and the spleen shows hemopoiesis. In these circumstances it is important to be sure that extramedullary hematopoiesis is not responsible for the splenomegaly if splenectomy is contemplated. Splenic puncture can provide such information and is a safeguard to be observed before splenectomy is attempted.

Splenic puncture affords an opportunity to study the mechanism of various types of phagocytosis occurring in the spleen; in addition, it may be of great help in bacteriologic investigations, especially where Histoplasma or Brucella may be involved. Finally, repeated punctures during treatment may have a place in evaluating therapy.

SUMMARY

A series of 46 splenic punctures is reported, and the technique employed is described. The procedure used has proved to be safe and helpful in diagnosis. Splenic puncture permits the making of an accurate diagnosis on occasions which otherwise might only be established by surgical operation or necropsy. Splenic puncture may enable one to reach a more accurate decision regarding the indications for or the contraindications to splenectomy in cases of splenomegaly.

DISCUSSION

Dr. Robert M. Zollinger, Columbus, Ohio: I suspect most surgeons feel as I do, that splenic puncture in hypersplenic disease is a procedure which is dangerous for them to attempt, and they would probably rather leave it to the internist, along with needle biopsies of the liver. So often the platelet level is low and the danger of hemorrhage correspondingly great. However, Dr. Ferris has shown that it can be safely done and valuable information gained, provided the biopsy specimen is interpreted by a competent hematologist.

Dr. Doan, at our institution, Ohio State University, feels there are very few indications for direct splenic diagnostic aspiration. He would utilize this procedure, as Dr. Ferris pointed out, only in cases of suspected osteofibrosis or osteopetrosis, with compensatory splenomegaly, in an effort to determine the ratio of blood production to blood destruction in the large spleen.

Only once in approximately 225 splenectomies for hypersplenism which we have performed in recent years has the hematologist felt that splenic biopsy was required for diagnostic purposes preliminary to splenectomy. In this case, after inconclusive cellular data on medical splenic aspiration, Dr. Doan asked that the splenic puncture be done after the abdomen was opened. He was unable again to make a decision after studying the biopsy material obtained by the needle aspiration. It was necessary to resort to a frozen section of a small triangular segment of splenic tissue to get an adequate histologic appraisal. From these studies he decided the spleen should be removed, and peripheral cytologic reequilibration did follow the splenectomy. It is his belief—and in this Dr. Ferris and he do agree—that in a few selected patients there is no other way to obtain the necessary information for rational therapy.

Of course, splenectomy for a variety of blood disorders is a common surgical procedure, and I personally feel that this paper is of particular value in calling to the attention of surgeons the detailed hematologic studies which may be necessary to determine the need for splenectomy.

The surgeon should not forget that results of splenectomy for hypersplenism are dependent for accuracy on the preoperative diagnosis, followed, of course, by a meticulous technique in the performance of the splenectomy.

CLINICAL ASPECTS OF ACUTE PERIPHERAL OLIGEMIA FROM PLASMA WATER AND SODIUM SALT LOSS

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ANN ARBOR, MICH.

THE UNCOMPENSATED loss of fluids from the gastrointestinal tract or the immobilization of significant amounts of extracellular fluid into body tissues or cavities produces a diminution of physiologically effective extracellular volume that may be characterized by concentration of the formed elements of the blood [1]; decrease in the circulating blood volume, the major portion of which is diminution of plasma volume [2]; increased blood viscosity,[3] and depletion of total body electrolyte, quantitatively, qualitatively, or both, according to the mechanism of loss.[4] If such a loss is permitted to progress in a relatively rapid manner, with concomitant inadequate replacement, the resultant oligemia may produce all variants of peripheral vascular insufficiency that, in important manifestations, resemble peripheral vascular insufficiency produced by hemorrhage or trauma, but differ as regards initiation, as regards certain clinical and laboratory findings, and, particularly, as regards definitive therapy. The first documentations of this concept were made over 120 years ago, when it was observed that patients in extremis from the purges of cholera had remarkable response to the parenteral administration of sodium salts and water.[5] Increasing progress in biochemical technics and continuing research have added greatly to our knowledge of disease states producing defects of extracellular fluid, but much remains to be learned.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 7, 1953.

From the Department of Surgery, University of Michigan. This work was supported by a grant from the John Harper Seeley Foundation.

1. Nadal, J. W.; Pederson, S., and Maddock, W. G.: Comparison Between Dehydration from Salt Loss and from Water Privation, J. Clin. Invest. **20**:691, 1941.

2. Marriott, H. L.: Water and Salt Depletion: Publication Number 32, American Lecture Series, Monograph in American Lectures in Physiology, edited by R. F. Pitts, Springfield, Ill., Charles C Thomas, Publisher, 1950.

3. Seligman, A. M.; Frank, H. A., and Fine, J.: Traumatic Shock: XII. Hemodynamic Effects of Alterations of Blood Viscosity in Normal Dogs and Dogs in Shock, J. Clin. Invest. **25**:1, 1946.

4. (*a*) Elkinton, J. R.; Danowski, T. S., and Winkler, A. W.: Hemodynamic Changes in Salt Depletion and in Dehydration, J. Clin. Invest. **25**:120, 1946. (*b*) Danowski, T. S.; Winkler, A. W., and Elkinton, J. R.: The Treatment of Shock Due to Salt Depletion: Comparison of the Hemodynamic Effects of Isotonic Saline, of Hypertonic Saline, and of Isotonic Glucose Solutions, ibid. **25**:130, 1946. (*c*) Elkinton, J. R.; Winkler, A. W., and Danowski, T. S.: The Importance of Volume and of Tonicity of the Body Fluids in Salt Depletion Shock, ibid. **26**:1002, 1947.

5. O'Shaughnessy, W. B.: Analysis of the Blood in Cholera, London M. Gaz. **9**:486, 1831-1832.

Vomiting, diarrhea, fistulous gastrointestinal tract drainage, indwelling gastric or enteric suction, loss of bile or pancreatic secretions, and profuse drainage from an ileostomy are all physiological aberrations in certain surgical patients that produce important loss of extracellular water and sodium without necessarily being associated with clinically significant loss of plasma protein or red blood cells. Indeed, if the loss is of great magnitude rapidly induced, a relative increase in red blood cell count, hemoglobin, hematocrit reading, and hyperconcentration of plasma protein may occur.[2] Surgical disease states such as peritonitis and intestinal obstruction, attended by large losses of sodium salts and water, can be associated with variable clinically significant losses of plasma protein and red blood cells (Table 1). Only hemorrhage can produce simultaneous equal and parallel loss of all components of the intravascular portion of the extracellular fluid (Table 2). All problems of extracellular fluid deficit, therefore, require individualization, all clinical and laboratory

TABLE 1.—*Constituents of Extracellular Fluid*

1. Formed blood elements (red blood cells, white blood cells, platelets)
2. Protein
3. Water
4. Electrolyte (90% sodium salts)
5. Hormone and enzyme systems

TABLE 2.—*Examples of Surgical Disease States Producing Varying Segmental Loss of Constituents of Extracellular Fluid*

Water and electrolyte loss without clinically significant loss of red blood cells and protein: vomiting, diarrhea, fistulous gastrointestinal tract drainage, intestinal intubation
Water and electrolyte loss with potential or actual important clinically significant loss of protein and red blood cells: Intestinal obstruction, peritonitis, burns, severe trauma, severe infection (gas gangrene, necrotizing fasciatis)
Parallel loss of all elements of intravascular portion of extracellular fluid: Hemorrhage

aids available being utilized, so that the varying degrees of segmental losses can be estimated with maximum accuracy. Only in this manner can the most suitable repair solution be chosen.

THE PATHOLOGIC PHYSIOLOGY OF SODIUM SALT DEPLETION

The resultant picture of sodium salt and water depletion depends upon (1) the rate of loss and composition of the body fluid, (2) the existing disease state, (3) the amount and composition of fluids parenterally administered, (4) the rate of potassium loss, and (5) the patient's general condition and duration of illness at the onset of such uncompensated loss.

Rapid and continued loss of large amounts of body fluids containing significant sodium concentrations may, in just a few hours, produce severe peripheral oligemic shock and even death from circulatory failure. The concept of a shift of fluid from the cells to buffer extracellular space deficit in acute sodium loss is, as a generalization, no longer tenable in the light of recent experimental work.[6] Provided that concentration of sodium salts does not become hypertonic, there is little reduction in intracellular fluid volume with rapid extracellular loss. On the contrary, if the

6. Holmes, J. H., and Painter, E. E.: Role of the Extracellular Fluid in Traumatic Shock in Dogs, Am. J. Physiol. **148**:201, 1947.

concentration of sodium salts falls because of continued extracellular fluid loss, water passes into the cells so that maximum isotonicity of body fluids may be maintained. It has been shown that under such circumstances the cells may be markedly overhydrated even though severe peripheral oligemic shock exists.[7] The composition of exogenous loss of gastrointestinal secretions varies, chiefly because of the relative amounts of sodium, chloride, and potassium in their electrolyte structure. As a general consideration, it may be stated that the higher the sodium concentration of lost secretions the greater will be the resultant defect of extracellular fluid. Water loss in excess of sodium salts may occur in surgical patients in whom the oral or parenteral water intake is less than the obligatory insensible loss. Experimentally produced water depletion, with comparable decline in extracellular volume produced by sodium salt depletion, does not produce peripheral vascular collapse, although cardiac output, mean arterial pressure, plasma volume, and circulation rate decline. Little protein, if any, disappears from the plasma.[4] Salt depletion, on the other hand, produces peripheral vascular insufficiency with a sharp decline of plasma volume, cardiac output, blood pressure, and circulation rate. Sodium salt depletion is also attended by a disappearance of protein from the plasma, the mechanism of which remains poorly understood.[8]

The surgical disease state producing an extracellular fluid deficit is of obvious importance, as it determines or has significant relationship to such variables as composition and rate of loss; nutritional status; attendant pathology, with its effects upon all physiological processes, and the nature of the corrective operative procedure. Of primary consideration when one is dealing with surgical conditions that may produce significant extracellular volume deficits is constant vigilance to detect early signs and symptoms of such deficits, because defects of equal magnitude may in one patient produce minimal symptoms while in another they may be responsible for clinically significant interference with adequate circulation.

The continued administration of glucose and water solutions during extracellular fluid depletion effected by the loss of sodium salts not only will result in further dilution of remaining extracellular electrolyte but will cause or augment intracellular edema.[7] Normally the total effective solute concentration of the extracellular volume is jealously guarded. As the salt concentration of extracellular fluid diminishes, the kidney apparently excretes water in order to maintain isotonicity in response to inhibition of the antidiuretic hormone.[9] It has been shown, however, that in patients with inadequately treated Addison's disease, certain patients with congestive heart failure in whom the serum sodium is lowered during treatment of their edema, and normal dogs depleted of extracellular fluid electrolyte, an abnormality of water excretion exists.[10] A mechanism which effects conservation of water irrespective of serum solute levels has been postulated. Isotonicity is sacrificed and water is retained in an attempt to expand volume when death threatens from vascular insufficiency. Even in the presence of a dilute serum a concentrated urine is excreted. This

7. Darrow, D. C., and Yannet, H.: Changes in the Distribution of Body Water Accompanying Increase and Decrease in Extracellular Electrolyte, J. Clin. Invest. **14**:266, 1935.

8. Nadal, Pederson, and Maddock.[1] Footnote 4.

9. Verney, E. B.: Absorption and Excretion of Water: Antidiuretic Hormone (Sharpey Schafer Memorial Lecture, Abridged), Lancet **2**:781, 1946.

10. Leaf, A., and Mamby, A.: Antidiuretic Mechanism Not Regulated by Extracellular Fluid Tonicity, J. Clin. Invest. **31**:60, 1952.

abnormal antidiuretic pattern is considered to represent continued activity of the supraopticohypophyseal antidiuretic system, and it is believed that the stimulus for posterior pituitary activity is an insufficiency of some function of volume in a crucial portion of the extracellular fluid volume, possibly intravascular. This situation probably can arise only when there is a low salt intake in association with unlimited oral intake or the parenteral administration of water.[10]

For the most part, large extracellular sodium salt depletions are associated with potassium deficits.[11] Relatively little is known, however, of the vagaries of the movement of potassium across cell membranes in response to various dehydrational states.[12] The continued loss of body fluids with a relatively high potassium content undoubtedly produces serum and cellular depletion of this electrolyte, which must be replaced if maximum therapeutic effectiveness of repletion therapy is to be obtained. The administration of sodium salts can greatly increase these losses of potassium.[13] Furthermore, it has been demonstrated that relative and absolute intracellular hypernatremia occurs during the administration of repair or maintenance sodium salt solutions. This condition can be prevented or corrected by the administration of potassium salts.[11] Such potassium losses are of little immediate concern in cases of acute dehydrational oligemic shock produced by the loss of extracellular fluid. After shock has been corrected and adequate urine output obtained, careful consideration must always be given the attendant potassium depletion, which may have been masked by the sodium salt depletion or possibly produced by the dilutional effect of sodium salt repair solutions.

Infants, the very old, and patients with prolonged or debilitating disease tolerate poorly sudden changes in extracellular fluid volume.[14] Postoperative care of patients in older age groups should always be orientated to the consideration that small losses of extracellular fluid may be productive of rather severe symptoms.

ISO-OSMOLAR ACUTE EXTRACELLULAR FLUID DEFICITS PRODUCED BY THE LOSS OF SODIUM SALTS AND WATER

Rapid loss of extracellular fluid containing essentially isotonic sodium salt and water may produce a severe depletion of plasma volume with relatively little change in the osmolar concentration of remaining electrolyte. Under these circumstances the passage of water from the extracellular space into the cells is apparently not of clinical importance. Laboratory determination of serum electrolyte concentrations may give normal results even though severe peripheral oligemia hypotension is present. Continued loss, however, when attended by inadequate replacement tends, for the most part, to produce a state of hypo-osmolarity even though it is not reflected by characteristic clinical symptoms.[15]

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11. Darrow, D. C.: Medical Progress: Body-Fluid Physiology; The Role of Potassium in Clinical Disturbances of Body Water and Electrolyte, New England J. Med. **242**:978 and 1014, 1950.

12. Elkinton, J. R.; Winkler, A. W., and Danowski, T. S.: Transfers of Cell Sodium and Potassium in Experimental and Clinical Conditions, J. Clin. Invest. **27**:74, 1948.

13. Berry, R. E. L.; Iob, V., and Campbell, K. N.: Potassium Metabolism in the Immediate Postoperative Period, Arch. Surg. **57**:470, 1948.

14. Bland, J. H.: The Clinical Use of Fluid and Electrolyte, Philadelphia, W. B. Saunders Company, 1952.

15. Moyer, C. A.: Fluid Balance: A Clinical Manual, Chicago, Year Book Publishers, Inc., 1952.

Signs and symptoms of acute rapid losses of extracellular fluid are principally related to depletion of the effective circulating blood volume, because of rapid contraction of plasma volume. As such losses continue, signs referable to interstitial fluid loss may become apparent (loss of skin turgor, furrowing of the tongue, loss of ocular tension, atonia of muscles, and ileus).

Table 3 outlines signs and symptoms produced by iso-osmolar acute extracellular fluid deficits.[16] Apathy, diminished affect, anorexia, nausea, weakness, and poor venous peripheral filling time may be observed with small deficits. As the loss of extracellular fluid approaches 20% of its effective volume, peripheral venous filling becomes progressively inadequate and pulse volume diminishes. Tachycardia may be present. The extremities are cool, and cyanosis may be observed in the nail beds. Faintness or syncope may result when the erect position is assumed. Losses greater than 30% may produce absence of peripheral venous filling, marked decrease of pulse volume or absence of peripheral pulses, and coldness and cyanosis of the extremities. Pressures in the brachial artery which had previously been unstable may progressively fall until a value for peripheral blood pressure is no longer obtainable. Depression of the sensorium and the gray-ashen appearance

TABLE 3.—*Signs and Symptoms of Extracellular Fluid Deficit of Iso-Osmolar Type*

10% Loss:	Apathy, anorexia, depression of thirst, diminished affect, weakness, slow peripheral venous filling, low body temperature
20% Loss:	Nausea and vomiting, refusal of food and water, ileus, progressive diminution of peripheral venous filling, orthostatic hypotension, tachycardia, syncope or dizziness upon assuming erect position, diminished skin turgor, and shrinkage of tongue
30% or Greater Loss:	Weak or absent peripheral pulses, progressive hypotension, cold extremities, facial suffusion with heightened coloring (dehydrational polycythemic flush), reduction in reflexes, hypostatic lividity, sunken soft eyeballs, atonic muscles, stupor, coma (until the agonal state is reached the sensorium may remain surprisingly intact, even when brachial artery pressure is absent, in salt-depletion peripheral oligemic shock)

of the face, however, may not occompany these deficits. It has been our repeated observation, in certain cases, that the sensorium remains intact, the patient's affect is minimally depressed, and reasonably complicated questions can be answered adequately, although the pressure in the brachial artery cannot be recorded. Furthermore, instead of a typical "shock" facies, there may actually be an increased suffusion of the face, with associated heightened coloring (dehydrational oligemic flush). This paradoxical facial appearance undoubtedly represents a transitory phase and is related to the relative polycythemia produced by hyperconcentration of the red blood cell mass. It is important, in that the seriousness of the extracellular fluid deficit may not be appreciated on casual examination because of the intact sensorium and normal or increased facial coloring. It fails to reflect, as regards the usual clinical concept, the severe depletion of intravascular fluid attendant on the absence of brachial artery pressure and peripheral pulses. Dehydrational polycythemic flush has not been observed in association with traumatic or hemorrhagic shock. Progressive loss of effective circulation and increasing anoxia can eventually produce a stupor, coma, and the ashen cyanosis commonly observed with other types of oligemic shock.

Laboratory signs are variable.[15] Levels of serum sodium, chloride, and carbon dioxide may be normal. Potassium concentration may be normal or increased.

16. Marriott.[2] Moyer.[15]

There is concentration of the formed elements of the blood, with a relative increase in hemoglobin and the hematocrit reading. The nonprotein nitrogen may be elevated. Hyperconcentration of the plasma proteins is commonly found. Slower loss of extracellular fluid may be associated with disappearance of plasma proteins at about the same rate as the salt and water loss.[4a,b] Blood viscosity rises.[3] The amount and specific gravity of the urine are variable. A high specific gravity tends to reflect the severity of the water deficit, but the excretion of relatively normal volumes of urine with a specific gravity of less than 1.020 has been observed. Red blood cells, albumin, and casts, if present, probably represent renal tubular irritation. Very little, if any, chloride is found in the urine as long as relative iso-osmolarity is preserved.

The following protocol presents an example of postoperative development of a severe extracellular fluid volume deficit of the iso-osmolar type as regards clinical aspects, laboratory findings, and therapeutic response.

CASE 1.—A. S. (University Hospital No. 732475), a 38-year-old white woman, was admitted to the University Hospital Dec. 12, 1952, with the complaint of backache and diarrhea of 10 years' duration. Previous sigmoidoscopy and a barium sulfate enema had revealed multiple polyposis of the colon. Numerous members of her family had the same condition.

At physcial examination the temperature was 98.6 F., the pulse rate 80, and the respiratory rate 20. The weight was 111 lb. (50 kg.) and the height 5 ft. 3 in. (160 cm.) The blood pressure was 120/70. The patient was well developed but thin. The remainder of the physical examination gave essentially negative results.

Sigmoidoscopic examination revealed studding of the rectal and sigmoid mucosa with reddened, edematous friable polyps. Several biopsy specimens were taken, and, although there was suggestive evidence of beginning infiltrative growth, a diagnosis of carcinoma could not be made. Use of a barium sulfate enema yielded typical findings of multiple polyps extending from rectum to cecum. On Dec. 19, a total removal of the colon and rectum was performed and the terminal ileum anastomosed to the distal ½ in. (1.27 cm.) of the rectum after removal of the mucosa. Subsequent examination of the specimen revealed a well-differentiated adenocarcinoma of the cecum in addition to the polyposis. A small Penrose drain was inserted for drainage of of the subperitoneal area through a stab wound just posterior to the anus. She received 1,000 cc. of whole blood during the operation, and this was followed by 1,500 cc. of 5% dextrose in distilled water. During the first 24 postoperative hours 500 cc. of urine was excreted and 500 cc. of intestinal contents was removed by long-tube suction. The day after operation she was given 2,000 cc. of 5% dextrose in distilled water and 500 cc. of Hartmann's solution.[17] During the same period 700 cc. of urine was excreted, 400 cc. obtained by intestinal suction, and 150 cc. passed through the anal ileostomy. Forty-eight hours after operation the patient was observed to be lethargic, but there was a definite suffusion of the face, with heightened coloring (dehydrational polycythemic flush). She was oriented and answered questions well. The hands were cold and the nail beds cyanotic. Filling of the veins on the dorsa of the hands was absent. The radial pulse was absent, and the brachial artery pressure could not be recorded. Tissue turgor was good (Table 4).

The hemoglobin content was 16 gm. A specimen of urine revealed a specific gravity of 1.015, a 1+ reaction for albumin, and a value for urine chloride by gross estimation, the Fantus test being utilized, of less than 2 gm. per liter. The sodium content was 136 mEq., potassium 6.9 mEq., CO_2 54 vol. %, chloride 85 mEq., and nonprotein nitrogen 77 mg. per 100 cc. A diagnosis of severe extracellular fluid deficit, iso-osmolar in type as regards its chief clinical and laboratory considerations, with associated relative concentration of the red blood cell mass, was made. During the next 12 hours she received 4,000 cc. of Hartmann's solution. At the end of four hours' administration of this solution the brachial artery blood pressure had returned to 118/82 and filling of peripheral veins had returned. Upon completion of repair of the extracellular defect,

17. NaCl 6 gm., sodium lactate 3.1 gm., KCl 0.3 gm., and $CaCl_2$ 0.2 gm., per 1,000 cc. of distilled water.

the hemoglobin content was 12.5 gm. Twenty-four hours later blood chemistry values were sodium 137 mEq., potassium 3.4 mEq., chlorides 87 mEq., carbon dioxide 62 vol. %, and nonprotein nitrogen 65 mg. per 100 cc.

The course during the next four days was satisfactory, although oral intake had to be supplemented occasionally by parenteral administration of fluids. On the eighth postoperative day ileal contents were observed to be draining from the posterior stab wound and probing revealed a dehiscence of the anastomosis. Almost simultaneously the patient bagan to have hallucinations and delusions. Blood chemistry studies revealed a sodium content of 124 mEq., potassium 5.6 mEq., chloride 101 mEq., carbon dioxide 41 vol. %, and nonprotein nitrogen 44 mg. per 100 cc. The hemoglobin content was 12.5 gm. The hyponatremic acidosis was treated by intravenous injection of Hartmann's solution and oral administration of an electrolyte solution containing 3 gm. of NaCl and 1.5 gm. of $NaHCO_3$ per liter.

TABLE 4 (Case 1).—*Postoperative Development of Severe Extracellular Fluid Deficit of Iso-Osmolar Type with Regard to Clinical and Laboratory Manifestation*

	Jan. 19	Jan. 20	Jan. 21	Jan. 22
Clinical Condition	Good	Postoperative condition apparently satisfactory	Patient lethargic; face suffused, with heightened coloring; venous filling absent; radial pulses and brachial artery pressure absent; hands cold and cyanotic; sensorium intact; tissue turgor good	Blood pressure and pulse stabilized; venous filling good
Intake	Whole blood 1,000 cc.; 5% glucose in water 1,500 cc.	2,000 cc. 5% glucose in water; 500 cc. Hartmann's solution	4,000 cc. Hartmann's solution	2000 cc. Hartmann's solution; oral intake 1,875 cc.; 6 gm. KCl given next 24 hours
Output	Urine 500 cc.; long tube 600 cc.	Urine 700 cc.; long tube 400 cc.; anal ileostomy 150 cc.	Urine 600 cc.; long tube 500 cc.; anal ileostomy 400 cc.	Urine 1,025 cc.; anal ileostomy 500 cc.
Laboratory Findings	Hgb. 12.9 gm.	.....	Na 136 mEq.; K 6.9 mEq.; Cl 85 mEq.; CO_2 54 vol. %; NPN 77 mg.; Hgb. 16 gm. Urine: S.G. 1,015; albumin 1+; Fantus test 2 gm./liter	Na 137 mEq.; K 3.4 mEq.; Cl 87 mEq.; CO_2 62 vol. %; NPN 65 mg.; Hgb. 12.5 gm.
Remarks	Day of operation: 1-stage removal of colon and rectum for multiple polyposis; carcinoma of cecum without nodal involvement, incidental finding; operation tolerated well; anal ileostomy performed	Progressive immobilization of extracellular fluid into peritoneal cavity, bowel lumen and wall	Severe peripheral oligemic shock treated with Hartmann's solution; blood pressure normal and venous filling returning within 4 hr.	Fall in concentrations of NPN, Hgb., and K; general condition satisfactory

On Jan. 6, 1953, an abdominal ileostomy was done without untoward event. The immediate postoperative course was characterized by disorientation and hallucinations despite what was thought to be adequate replacement of water, electrolyte, and blood. On Jan. 13, the patient suddenly became dyspneic and cyanotic and died. The only significant finding at autopsy was moderate cerebral edema. According to gross examination the brain was wet but was without other significant change. A silver carbonate preparation showed a very severe proliferation and clasmatodendrosis of the astroglia, and advanced rarefaction of the cytoarchitecture, with disintegration of the neurones and reduction and edema of the cylinders. The oligodendroglia was swollen and partly destroyed. Microglia (as usual in cases of this type) was not conspicuous. It was felt that these changes probably represented acute disintegration of the brain of toxic etiology.

The precipitation of an extracellular fluid deficit of this magnitude during a short period of 48 hours was in part produced by external loss, which was partially covered by parenteral administration of salt solution. Of greater importance, however, was the loss of fluid into the abdominal wall, peritoneal cavity, bowel wall, and intestinal lumen produced by operative trauma and ileus. This was larger

than reasonably could have been anticipated. Undoubtedly all elements of extracellular fluid were physiologically immobilized, but the loss of sodium salts and water dominated the clinical picture. Although an excellent therapeutic result was achieved by the administration of a sodium salt solution containing no colloid, consideration of replacement of acute protein deficits that may be attendant is necessary. Rapid salt depletion shock of this type is often accompanied by relative hyperconcentration of red blood cells and the plasma proteins.[1] It is imperative, therefore, that first consideration be given to replacement of the salt water portion of the extracellular fluid. Reevaluation of the clinical status following such restoration permits a more accurate estimate of the need for plasma and/or blood transfusions.

Heightened color of the face (dehydrational polycythemic flush) in severe peripheral oligemic states occurs when the primary defect is mainly extracellular salt water. It is important because the patient's "good color" is not ordinarily associated with severe peripheral oligemia shock.

It has been repeatedly observed that laboratory determination of serum electrolytes fails to reflect the true status of the extracellular fluid volume.[15] The serum sodium level of 136 mEq. was unchanged after repletion therapy. A blood chloride value of 85 mEq. is quite compatible with the physiological hypochloremia observed in many patients in the immediate postoperative period. No change was observed following repletion. The CO_2 levels before and after repletion are of little clinical significance.

Large losses of sodium salts are, for the most part, associated with increases in the blood nonprotein nitrogen. It is a mistake to consider abnormally high blood urea values as evidence of retention in the concept that urea is not being adequately eliminated. Urea is removed by the cooperation of three factors: plasma urea concentration, volume of the glomerular filtrate, and work.[18] If there is a diminution of contribution of one of these factors, then the other two must increase in order to achieve the same end-result: excretion of urea at the rate at which it is produced. Glomerular filtration decreases in conditions of shock or diminution of sodium salt concentrations. The increase of blood urea, therefore, represents a compensatory mechanism to obtain its maximal renal excretion.[18]

The increased potassium concentration (6.9 mEq. in this case) is probably not related to diminished glomerular filtration, because even in advanced renal disease potassium clearance may be well maintained.[14] Increased serum concentrations of potassium have been observed in shock, anoxia, dehydration, and sodium salt deficits.[11] With the exception of hyperpotassemia produced by hypertonicity of extracellular sodium salts, the mechanisms responsible for serum hyperkalemia remain poorly understood.[12] A drop of serum potassium to a level bordering on hypopotassemia (3.4 mEq. in this case) following reexpansion of the extracellular fluid volume has been a commonly observed phenomenon and has been related to the increase in extracellular fluid volume, to increase in organic constituents of the cells accompanied by higher amounts of cellular potassium, and to alterations in the activities and the structures of cells that lead to increase in cellular potassium.[11]

18. Newburgh, L. H., and Leaf, A.: Significance of the Body Fluids in Clinical Medicine, (American Lectures in Physiology, No. 69), Springfield, Ill., Charles C Thomas, Publisher, 1950.

The onset of mental aberrations in patients receiving fluids parenterally should be considered a complication of such fluid therapy until proved otherwise. The onset of delusions and hallucinations on the eighth postoperative day was attended by a hypotonic dehydrational acidosis. No improvement in the mental status was observed following correction of this abnormal electrolyte pattern. Although a diagnosis of functional psychosis was entertained, it was felt that the disorganization of this patient's psyche was importantly related to central nervous system cellular metabolic changes produced either by repeated insults from fluid disequilibrium states or by factors which could not be clearly identified. The second operation (abdominal ileostomy) was tolerated well as regards her somatic response, but the mental status remained unimproved. The etiology of acute brain disintegration with attendant sudden death is unknown. It has been observed in patients dying from

TABLE 5.—*Mechanism of Production of Hypo-Osmolarity of Extracellular Fluid*

Loss of Extracellular Fluid	
↓	↓
Loss of sodium salts and water	Loss of sodium salts and water
↓	↓
Initial renal adjustment to maintain isotonicity of remaining effective extracellular fluid	Hyperconcentration of plasma proteins
↓	↓
Decrease in sodium salt concentration	Movement of water from interstitial fluid compartment into plasma
↓	↓
When exogenous source of water is available water is retained to maintain volume and isotonicity is sacrificed	Further dilution of serum electrolyte
↓	
Intracellular overhydration by movement of water from extracellular to intracellular fluid compartment to maintain isotonicity of body fluids	
↓	
Marked symptomatic cell overhydration may be present, with severe salt-depletion shock	

status epilipticus, acute psychosis, severe allergic states, ulcerative colitis, uremia, and severe metabolic disorders.[19]

HYPO-OSMOLAR EXTRACELLULAR FLUID DEFICITS PRODUCED BY LOSS OF SODIUM SALTS AND PLASMA WATER

There is ample proof that removal of sodium, in some circumstances, does not remove a proportional amount of water. As the concentration of the extracellular space falls, water moves into the cells until osmotic equilibrium between extracellular and intracellular spaces is accomplished. If the loss of sodium salts proceeds at a rate that prohibits the immobilization of plasma proteins, there is hyperconcentration of protein with resultant increase in colloid osmotic pressure. As a result, water moves from the interstitial fluid compartment into the intravascular space. In this manner blood volume may be partially buffered at the expense of the interstitial fluid [18] (Table 5).

When an exogenous source of water is available, such as unlimited oral intake or parenteral adminstration of dextrose and water during continued loss of sodium salts, the kidney initially attempts to maintain isotonicity. As the threat of death

19. Scharenberg, K.: Personal communication to the author.

from circulatory failure increases, isotonicity is sacrificed and water is retained in the interest of maintaining blood volume. The mechanism for the production of this physiological phenomenon is not known. It has been suggested that it represents a continued stimulus for posterior pituitary activity possibly related to volume function insufficiency of some segment of the extracellular fluid.[10] In acute conditions the progression of intracellular overhydration may produce significant clinical findings.

The signs and symptoms of extracellular volume deficit remain essentially unchanged. Clinically, initial manifestations of serious cellular overhydration are related to the central nervous system. Disorientation, restlessness, muscle twitchings, hyperactivity of tendon reflexes, and increase in spinal fluid pressure may be observed. Convulsions, particularly in children, may be the initial sign of overhydration. Papilledema, attempts at the extrarenal excretion of water, and intracutaneous edema may result if the condition persists.[15]

Laboratory determination of plasma sodium, chloride, and CO_2 may reveal a marked decrease. Potassium content is varied. Hemoglobin content, hematocrit reading, level of plasma proteins, and red blood cell count are also variable. Urinary output and specific gravity show no constant pattern. Little or no urine chloride is found.

The following protocol is representative of the postoperative development of a marked hypo-osmolar extracellular fluid deficit.

CASE 2.—M. B., (University Hospital No. 494046), a 54-year-old Negro woman, was admitted to the hospital Jan. 14, 1953. Her present illness began about four months previously, with the onset of repeated paroxysms of coughing. At approximately the same time she observed a nontender mass, about 2 cm. in diameter, in the left supraclavicular region. An x-ray of the chest was normal, and the patient was treated symptomatically for the next three months. A second x-ray of the chest then revealed a mass in the left lung field and she was referred to the university hospital.

Physical examination revealed a well developed and well nourished Negro woman appearing neither acutely nor chronically ill. The blood pressure was 118/84, pulse rate 96, respiratory rate 20, and temperature normal. There was a firm, movable mass measuring 4 by 5 cm. in the left supraclavicular area. Breath sounds were depressed over the lower lobe of the left lung. The remainder of physical examination gave negative results. The urine was normal. The hemoglobin content was 12.9 gm. and the white blood cell count 8,150. An x-ray of the chest was reported as showing a suggestion of a tissue mass at the base of the left side of the neck. There was a rounded density 4.5 cm. in diameter just lateral to the superior pole of the left hilus. A tentative diagnosis of bronchogenic carcinoma with metastatic involvement of lymph nodes of the left supraclavicular group was made. Bronchoscopy gave negative results, and no acid-fast bacilli were found on a smear made from concentrated specimens of sputum and gastric juice. The mass in the left supraclavicular region was excised and reported as a poorly differentiated medullary carcinoma, histologically compatible with origin in the bronchus.

Three days after admission the patient began to complain of left upper-quadrant pain. Urine examination revealed 10 to 12 white blood cells per high-power field, bacteria, a specific gravity of 1.023, a pH of 5.5, and a 1 + reaction for albumin. Cultures of the urine were made, the clinical impression being that a mild urinary tract infection was present.

The following morning the patient continued to complain of left upper-quadrant pain, refused to eat, and began vomiting. Examination of the abdomen showed some tenderness in both lower quadrants. A long tube was passed and the patient maintained on parenterally administered fluids; 2,000 cc. of 5% dextrose in water, 1,500 cc. of Hartmann's solution, and 1,000 cc. of Ringer's solution with 4 gm. of KCL were administered. During this period 650 cc. of urine was excreted, with repeated specimens showing a high specific gravity. The value for serum amylase was 95 units, the nonprotein nitrogen 69 mg. per 100 cc., and the CO_2 48

vol. % The following day the patient was confused and restless. A flat plate of the abdomen was normal, and the physical findings on abdominal examination were essentially unchanged. During this period she received 1,000 cc. of 5% dextrose in water and 1,000 cc. of Hartmann's solution. The blood pressure began to rise, reaching a maximum at 210/120, and parenteral administration of fluids was discontinued. She excreted 1,000 cc. of urine and put out 500 cc. of drainage through the Cantor tube.

During the next 24 hours her condition became rapidly worse. The blood pressure fell to 150/100, disorientation and restlessness became marked, and abdominal examination revealed tenderness, rebound tenderness, and moderate rigidity. Urine output was inaccurately determined, but 600 cc. of dark-brown material had drained through the Cantor tube. The value for serum amylase was 104 units, nonprotein nitrogen 47 mg. per 100 cc. and CO_2 48 vol. %. A diagnosis of an acute surgical abdominal condition, probably from mesenteric vascular occlusion, was made. At operation the right colon and all but the proximal 12 in. of the small bowel were seen to be either frankly gangrenous or pregangrenous. The infarcted bowel was resected and continuity of the intestinal tract reestablished by anastomosis of the proximal part of the jejunum to the left side of the transverse colon; 1,000 cc. of whole blood was administered during the operation and was tolerated surprisingly well. Upon recovery from anesthesia the patient complained of pain in the right leg. Examination revealed absence of femoral and peripheral pulses. It was felt that embolization of the right iliac artery had occurred (Table 6).

During the first 24-hour postoperative period she became progressively disoriented, and muscle twitchings developed. Extreme restlessness necessitated restraint; 2,000 cc. of 5% dextrose in water and 1,000 cc. of Hartmann's solution were administered; 400 cc. of urine was excreted and 700 cc. of drainage obtained through the Cantor tube. The following day, by gross oversight, only 2,000 cc. of dextrose in water was administered. The serum sodium was 130 mEq. and potassium 3.6 mEq. She became incontinent of liquid rectal fecal drainage.

Progressive oliguria was approaching anuria by the 60th postoperative hour. The face was ashen. Peripheral pulses and venous filling were absent. Brachial artery pressure was absent. Examination of the blood revealed hemoglobin 14 gm., sodium 103 mEq., chloride 75 mEq., potassium 4.8 mEq., CO_2 63 vol. %, and nonprotein nitrogen 137 mg. per 100 cc.

Dramatic results followed rapid administration of 1,000 cc. of a 2% sodium chloride solution. The blood pressure returned to 118/86, the radial pulse was 80, urine output sharply increased, and there was marked improvement as regards of restlessness and disorientation. After completion of administration the hypertonic saline solution, the blood chloride was 101 mEq. and CO_2 43 vol. %. Repair of the extracellular defect was then continued with 2,000 cc. of Hartmann's solution, 500 cc. of whole blood, and 1,000 cc. of 5% dextrose in water. During the following 36 hours the patient excreted 1,400 cc. of urine, and blood chemistry values at that time were sodium 144 mEq., chloride 102 mEq., potassium 3.9 mEq., CO_2 56 vol. % calcium 9.7 mg. per 100 cc., and nonprotein nitrogen 168 mg. per 100 cc. Despite improvement in her condition, apparent arterial embolization or thrombosis of the left arm occurred on the fifth and of the left leg on the sixth postoperative day. On the seventh day it was felt that cerebral embolization or thrombosis had occurred, and she died on the eighth day after operation. The immediate cause of death as thought to be a cerebrovascular accident. Autopsy revealed the anastomosis to be intact. There was extensive generalized arteriosclerotic cardiovascular disease with mural thrombi in the abdominal aorta and thrombi or emboli in the right and left iliac arteries, superior mesenteric artery, and left axillary artery.

The rapid loss of gastrointestinal contents and the administration of dextrose and water with inadequate sodium salt replacement precipitated not only salt-depletion peripheral oligemic shock but a severe hypo-osmolarity of remaining electrolyte, as manifested clinically by symptoms referable to edema of the cells of the central nervous system and laboratory findings of a serum sodium level of 103 mEq. and a chloride level of 75 mEq. In this type of case restoration of iso-osmolarity and correction of severe acid-base imbalance should be accomplished before replacement of the volume deficit. A 2% NaCl solution was chosen for initial administration

TABLE 6 (Case 2).—*Postoperative Extracellular Fluid Deficit of Hypo-Osmolar Type*

	Jan. 9	Jan. 20	Jan. 21	Jan. 22	Jan. 23
Clinical Condition	Disorientation, severe abdominal pain, tenderness, rebound tenderness, rigidity	Disorientation improved but right leg became painful and cold	Progressive disorientation, muscle twitching	Marked disorientation and muscle twitching; peripheral venous filling absent; pulses and brachial artery pressure absent; extremities cold; face ashen	Disorientation improved; venous filling present
Intake	Hartmann's solution 2,000 cc.; whole blood 1,000 cc.	2,000 cc. 5% glucose in water; 1,000 cc. Hartmann's solution	2,000 cc. 5% glucose in water	1,000 cc. 2% NaCl; 2,000 cc. Hartmann's solution; 1,000 cc. 5% glucose in water; 500 cc. whole blood	1,000 cc. Hartmann's solution; 2,000 cc. 5% glucose in water with 6 gm. KCl
Output	Urine, severe oliguria; long tube 600 cc.	Urine 400 cc.; intestinal 700 cc.	Urine 250 cc.; long tube 175 cc.; patient incontinent of liquid rectal drainage	Urine 170 cc.; liquid rectal drainage	Urine 1,400 cc.
Laboratory Findings	Amylase 104 units; W.B.C. 41,000; CO_2 48 vol. %; NPN 47 mg.	.....	Na 130 mEq.; K 3.9 mEq.	Na 103 mEq.; K 4.8 mEq.; Cl 75 mEq.; CO_2 63 vol. %; Ca 10.6 mg.; NPN 137 mg.; Hgb. 14 gm.; CL 101 mEq. } after 1,000 cc. CO_2 43 vol. % } 2% NaCl	Na 144 mEq.; Cl 102 mEq.; CO_2 56 vol. %; K 3.9 mEq.; Ca 9.7 mg.; NPN 168 mg.
Remarks	72-hr. history of progressive abdominal pain and tenderness; right colon and all but proximal 12 in. of small bowel removed at laparotomy because of superior mesenteric artery occlusion	Postoperative condition unexpectedly good, but embolization of right iliac artery occurred	Administration of glucose in water alone was serious oversight, as symptoms suggested sodium salt hypo-osmolarity	Severe hypo-osmolar sodium salt deficit; return of body pressure to 118/86, drop of pulse to 80, and increased urine output noted during administration of hypertonic saline; marked improvement in disorientation	Blood pressure and pulse stabilized; blood chemistry essentially normal, except high NPN; patient remained disorientated; embolization of left axillary artery occurred, followed by embolization of right axillary artery the next day; death 8th postoperative day from cerebral embolus

because of the relatively normal CO_2 concentration. If severe hypo-osmolarity is accompanied by a large CO_2 deficit, then administration of ⅓ M sodium lactate may be indicated as the initial repair solution. The volume deficit of extracellular fluid can then be corrected with Hartmann's solution. The administration of colloid, either as whole blood or as plasma, has great benefit in this type of deficit,[20] as it not only aids in a more effective replacement but provides added insurance of a stable repair.

A gradual decrease in the total effective extracellular solute may produce marked hypo-osmolarity of the extracellular fluid without remarkable signs of cellular overhydration. This sequence is apparently accomplished by readjustments between intracellular and extracellular compartments, so that isotonicity of all body fluids is reached but at a lower concentration of total body electrolyte.[14] For the most part this situation has been observed in debilitating illness, usually associated with malnutrition.[21] Although this type of hypotonic dehydration proceeds at a slower rate, the end-result of the defect is quite capable of eventually producing salt-depletion dehydrational shock. Two considerations are of importance when one is dealing with this type of condition: First, often a marked oliguria and high level of nonprotein nitrogen are present. It is essential that the sodium salt deficit be corrected and "forced diuresis" avoided as the initial consideration of treatment. Dangerous cellular overhydration may be produced if water is administered parenterally without correction of the electrolyte deficit. Second, trauma or hemorrhage is poorly tolerated. Correction of electrolyte and water depletion and if possible betterment in nutrition should be accomplished before any operative procedure is carried out. Careful attention should be given potassium replacement, as this defect may be of considerable magnitude.

The following case history presents many of the clinical aspects of this type of salt depletion.

CASE 3.—W. G., (University Hospital No. 742034), a 28-year-old white married housewife, was admitted for the first time to University Hospital Dec. 19, 1952, with the chief complaint of pain in the abdomen. She had been well until Nov. 16, when generalized abdominal pain, distention, nausea, and vomiting developed. A diagnosis of intestinal obstruction was made and immediate laparotomy carried out. The terminal portion of the ileum had herniated through a defect in the broad ligament, with about 3 ft. (91 cm.) of small bowel rendered gangrenous by strangulation. She had had a uterine suspension about a year previously. The gangrenous small bowel was resected, but it was thought unwise to reestablish continuity of the gastrointestinal tract. A double-barreled ileostomy was brought out through the abdominal wound. The uterus was observed to be about the size of that in a three-month pregnancy.

During the five weeks following operation very little food and only occasional liquids were retained. She lost a great deal of weight, constant abdominal and back pain developed, and she noticed progressive difficulty in passing urine. During the 24 hours before her second admission she passed no urine at all. She was referred to the University Hospital, as it was thought that the pregnancy endangered her life and should be interrupted.

Physical examination revealed a well-developed, emaciated young woman who appeared acutely and chronically ill. She was well orientated but tended to be negativistic and uncooperative during examination. The temperature 99.2 F., the pulse rate 130, and the respiratory rate 20. Blood pressure was 80/68 in the right brachial artery, reclining position.

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20. Winkler, A. W.; Danowski, T. S., and Elkinton, J. R.: The Role of Colloid and of Saline in the Treatment of Shock, J. Clin. Invest. **25**:220, 1946.

21. Sims, E. A.; Welt, L. G.; Orloff, J., and Needhan, J. W.: Asymptomatic Hyponatremia in Pulmonary Tuberculosis, J. Clin. Invest. **29**:1545, 1950. Bland.[14]

The pulse volume was diminished. There was evidence of recent weight loss. Venous filling of the dorsa of the hands was almost absent; the extremities were cold and the nail beds cyanotic. There was marked loss of tissue turgor, and the eyes appeared sunken. A badly infected lower midline abdominal incision was present, through which protruded two loops of bowel, one of them extruding apparent small-bowel contents. The skin about the abdominal wound was macerated and severely irritated from constant bathing in intestinal secretions. Pelvic examination revealed a mid-line mass, which was thought to be a five-month-pregnant uterus.

The hemoglobin content on admission was 11 gm., and the white cell count 16,400. Bladder catheterization produced 300 cc. of grossly infected urine, which was acid in reaction, with a specific gravity of 1.008, and a reaction for albumin of 2 +, and was loaded with white blood cells and bacteria. Urine cultures were done. An x-ray of the chest was normal, and a flat plate of the abdomen revealed only the large uterus, with suggestive signs of an intrauterine fetus. The serum sodium content was 112 mEq., potassium 6.3 mEq., chloride 70 mEq., and CO_2 41 vol. %. The level of nonprotein nitrogen was 226 mg., total serum proteins 7.7 gm., albumin 4.2 gm., and globulin 3.5 gm. per 100 cc., with an albumin-globulin ratio of 1 : 2. Because of the high nonprotein nitrogen, history of progressing oliguria, and marked lowering of serum sodium, chloride, and CO_2 content, it was felt that restoration of osmolarity should be accomplished before repair of the deficit was begun. She was given 300 cc. of a 2% sodium chloride solution and 300 cc. of a ⅓ M sodium lactate solution. These were followed by 2,000 cc. of Hartmann's solution and 500 cc. of whole blood. The most striking features of the administration of hypertonic sodium chloride and lactate solutions were a sharp increase in urine output, 700 cc. being excreted during and shortly after administration, and a return of the blood pressure to 110/78. Blood chemistry studies made immediately after completion of the administration of hypertonic salt solutions revealed a value for chloride of 76 mEq. and for CO_2 of 47 vol. %. The improvement in clinical condition was of greater magnitude than might have been anticipated from the moderate increase in chloride and CO_2 content. Twenty-four hours after completion of restorative therapy the chemistry values were sodium 132 mEq., potassium 4.6 mEq., chloride 81 mEq., CO_2 54 vol. %, and nonprotein nitrogen 198 mg. per 100 cc. Despite 500 cc. of whole blood the hemoglobin had dropped to 10.0 gm. Signs of peripheral oligemia decreased, with a return of venous filling, warmth, and good color to the extremities.

Although this patient presented no further serious fluid-imbalance problem, her nutritional status continued poor. It was necessary to supplement her meager oral intake with periods of continuous gavage, a small indwelling plastic tube in the stomach being utilized, with administration of high-caloric, high-protein liquid feedings, repeated blood transfusions, and occasional parenteral administration of fluids.

With this program the weight increased from 87 to 92 lb. (39 to 42 kg.). Examination with a barium sulfate enema gave negative results and injection of the loops of ileum with radiopaque substance showed the fistula to be low in the ileum. On Jan. 21, 1953, operation was performed through a left transverse incision made just above the umbilicus. The small bowel was divided about 12 in. (30 cm.) proximal to the fistula, and a right ileotransverse colostomy made between the proximal end of the ileum and side of the transverse colon. The distal part of the ileum was closed and dropped back into the abdomen. The postoperative course was entirely uneventful, and the patient was discharged from the hospital eight days later, tolerating a full diet and gaining weight and strength rapidly.

The subsequent course has been satisfactory. Resection of the ileal fistulae will await maximum healing of the abdominal wall and satisfactory weight and strength gain, a period usually requiring 6 to 12 months.

The severe hypo-osmolarity of sodium chloride was not reflected by symptoms referable to overhydration of the cells of the central nervous system. Because of the deficit of CO_2 content, 300 cc. of a ⅓ M solution of sodium lactate was given simultaneously with 300 cc. of 2% NaCl. Their administration was followed by excretion of 700 cc. of urine, a return of the blood pressure to 110/78, and improvement in peripheral circulation. The blood chloride rose to 76 mEq. and the CO_2 to

47 vol. %. The clinical improvement, however, was considerably better than the blood chemistry findings might suggest. After the administration of 2,000 cc. of Hartmann's solution and 500 cc. of whole blood, the serum sodium was only 132 mEq. and the chloride 81 mEq. It has been repeatedly observed that in patients whose disability and malnutrition are of considerable extent the improvement of clinical status is not always reflected in a rapid return of the extracellular electrolytes to normal levels. Improvement in nutrition is usually paralleled by the return of the electrolytes to accepted normal values.

The transfusion of whole blood is an important adjunct in the treatment of sodium salt deficits [20] and is mandatory in almost all cases of the severe hypo-osmolar type of deficit. The primary defect, however, is the loss of sodium salts and water, and their replacement should be accomplished first. The use of whole blood alone to correct sodium salt deficits not only is unphysiological but may be attended by undesired complications.

CASE 4.—C. B., (University Hospital No. 741988), a 16-year-old white girl, was admitted to the University Hospital Jan. 7, 1953, complaining of severe abdominal pain and vomiting of 48 hours' duration.

On physical examination she appeared acutely ill. The facies were moderately cyanotic. She was well oriented. The temperature was 102.4 F., pulse rate 120, and respiratory rate 20. The extremities were cold and cyanotic, and peripheral venous filling was poor. The pulse volume was diminished. Brachial artery pressure was 90/?. Examination of the abdomen revealed moderate distention, with associated generalized tenderness and rigidity. There was a well-healed right lower pararectus scar resulting from appendectomy and removal of an ovarian cyst in April, 1952. There were a small amount of purulent vaginal discharge and some ooze of blood from the cervix. Rectal examination gave negative results.

A scout film of the abdomen was interpreted as showing extreme gastric dilatation, with some gas in the small bowel but without an obstructive pattern. The hemoglobin content was 14 gm. and the white blood cell count 45,000, the urine was acid in reaction, the specific gravity 1.015, the reaction for albumin 1 +, and microscopic examination negative. The value for serum amylase was 451 units. The blood chloride level was 99 mEq. and the CO_2 38 vol. % (reported subsequent to operation).

During physical examination the patient went into profound shock, the blood pressure being almost unobtainable. Blood transfusions were started immediately, and during the next five hours 2,500 cc. of blood was given before the blood pressure became stabilized at 120/100. The pulse rate increased to 132. A hemoglobin determination at this time revealed it to be 22 gm. The patient appeared intensely plethoric. A long tube was passed and 600 cc. of brown fluid removed from the stomach. A diagnosis of perforated abdominal viscus was made, and at laparotomy the terminal 3 ft. (91 cm.) of ileum was seen to be gangrenous, having been strangulated by adhesions apparently formed by the previous operation. Resection of the diseased bowel was carried out and continuity of the intestinal tract restored by ileoascending colostomy. Twelve hours after operation the hemoglobin content was 16.5 gm., and the patient was still plethoric in appearance. About 48 hours after operation she became moderately jaundiced. The jaundice did not significantly affect the postoperative course, however, as convalescence was otherwise uneventful, and at no time was there indication of disturbance of renal function. At the time of discharge from the hospital, eight days after operation, the hemoglobin content was 15.5 gm., and the jaundice was clearing rapidly. Subsequent to discharge the patient's condition has remained satisfactory.

It is not unreasonable to assume that a diminution of plasma volume rather than the red blood cell mass was the most important cause of the peripheral oligemic hypotension. Attempts to correct the diminished blood volume with whole blood brought a return to satisfactory blood pressure but the resultant marked polycythemia, as manifested by the increase of hemoglobin from 14 to 22 gm., after

2,500 cc. of whole blood had been administered, was an undesirable corollary. The ability of the cardiovascular dynamics of this young patient to adjust to this unphysiological situation was importantly related to the fact that no serious complication occurred. Overtransfusion of red blood cells fortunately made little difference in the subsequent course of her illness. The judicious combination of administration of Hartmann's solution with whole blood transfusion not only would obviate the hazards of overtransfusion but would provide a more physiological and secure repair of the extracellular volume deficit.

Patients in the older age groups may poorly tolerate whole blood transfussions for correction of extracellular volume defects that are principally of water and electrolyte.

CASE 5.—J. G., a 68-year-old white housewife, was seen in consultation at an outstate hospital. This patient had undergone a resection of the lower portion of the esophagus and upper part of the stomach for carcinoma. Her postoperative course had been uneventful until the fifth postoperative day, when she became lethargic and orthostatic hypotension developed, with syncope, cold hands and feet with mild cyanosis, and markedly diminished peripheral venous filling. She was given 500 cc. of whole blood and another 500 cc. on the following day. Shortly after completion of the second transfusion the patient became dyspneic and cyanotic and râles developed at the bases of both lungs. A diagnosis of acute pulmonary edema was made, and venoclysis of 500 cc. of blood and rotating tourniquets successfully relieved the condition. Examination of this patient's record revealed that just prior to the first transfusion her hemoglobin was 17.5 gm. and the specific gravity of the urine 1.027. The defect in her extracellular fluid volume, therefore, was not a lack of red blood cell mass but a diminution of sodium salts and water. The administration of whole blood under these circumstances had precipitated acute cardiopulmonary distress. The patient was given 2,000 cc. of Hartmann's solution, with good restoration of the peripheral venous filling, a return of warmth to her extremities, and disappearance of the orthostatic hypotension.

When indicated, the administration of small repeated transfusions to elderly surgical patients is of great benefit. If, however, the primary defect of a diminished blood volume is a contracted plasma volume secondary to loss of sodium salts and water, transfusions of whole blood may not be well tolerated. Findings of a hemoglobin content of 17.5 gm. (Patient J. G.) and a urine specific gravity of 1.027, with associated clinical evidence of extracellular fluid volume loss, should be interpreted as being highly suggestive that an important segmental loss of sodium salts and water is the basic pathology. Whole blood transfusions were followed by serious complications. Subsequent administration of Hartmann's solution produced an excellent clinical response.

Blood viscosity may be significantly related to tolerance of whole blood transfusions in this type of dehydration. It is known that depletion of extracellular electrolyte and water can produce increased blood viscosity.[3] Experimentally it has been demonstrated that increased blood viscosity does not necessarily increase the work of the heart, as the total peripheral resistance adjustment may preclude the need for greater cardiac output or higher blood pressure.[3] Dehydrational oligemia, however, is accomplished by peripheral compensatory vasoconstriction because of diminished blood volume. Variations in peripheral resistance may, therefore, lose their elasticity. Under such circumstances it is not inconceivable that the administration of whole blood would not significantly decrease high plasma viscosity and that with the attendant inelastic peripheral resistance the work of the heart would be increased. This demand for increased cardiac effort would be poorly tolerated

by elderly patients with advanced myocardial fibrosis or arteriosclerotic coronary disease. Because the elderly patient is increasingly sensitive to small changes in all components of the extracellular fluid, the importance of correct identification of segmental defects and the proper choice of repair solutions cannot be overemphasized.

SUMMARY

Severe deficits of effectively circulating extracellular fluid may be produced by the extrarenal loss of body fluids characterized primarily by loss of sodium salts and water without clinically significant loss of plasma proteins or red blood cells. Continued loss may result in peripheral oligemic insufficiency that clinically resembles hemorrhagic or traumatic shock.

Rapid loss of body fluid resembling serum in electrolyte structure produces an iso-osmolar type of deficit, with increase in the relative concentrations of red blood cells and plasma proteins. Blood electrolyte values may be essentially normal.

The clinical picture and significance of the dehydrational polycythemic flush has been discussed.

Repair of iso-osmolar defects is best effected by repair of the salt-water defect with Hartmann's solution, added security of the repair being provided by whole blood transfusions. As in all salt and water defects, the amount of repair fluid adminstered is dependent upon the estimated percentage of extracellular fluid lost, body weight, clinical response to repletion, and a careful evaluation and interpretation of adjunctive laboratory data.

Extracellular fluid defects with associated hypo-osmolarity of the sodium salts may be attended by symptoms referable to overhydration of the cells, particularly those of the central nervous system. Repair of this type of defect is best initiated with 2% NaCl and/or ⅓ M sodium lactate, according to the CO_2 content of the plasma. Restoration of iso-osmolarity of remaining effective extracellular fluid volume can then be followed by the correction of the deficit with administration of Hartmann's solution and blood transfusions.

The undesirability and hazards of treatment of extracellular salt water defects by whole blood transfusions alone have been discussed.

DISCUSSION

DR. WALTER G. MADDOCK, Chicago: The vast majority of water and electrolyte problems are relatively simple and easily corrected. To handle the few difficult cases, one needs just the sort of information furnished by this excellent study of Dr. Berry's. Rapid loss of an extracellular fluid containing isotonic sodium chloride and water can be expected to change very little the osmolar concentration of the remaining electrolytes, with the result that laboratory determinations of serum electrolytes may be normal and thus poorly indicate the serious extracellular fluid deficit. Of great importance in suspecting the depleted state are the clinical signs and symptoms of reduced circulating blood volume with paradoxically the laboratory finding of relative hyperconcentration of red blood cells and plasma proteins. I am going to be on the lookout for the "increased suffusion of the face with associated heightened coloring" in this condition, as described by Dr. Berry.

A slower loss of sodium chloride and water, or more time to adjust to an acute loss, results in a hypo-osmolar extracellular fluid deficit. Signs of reduced circulating blood volume, such as lowered blood pressure, are present, along with central nervous-system depression and

muscular irritability. The laboratory studies here show the loss of sodium chloride by reports of low determinations of plasma sodium chloride and carbon dioxide. The cellular blood findings are variable. Initial corrective fluid here should be hypertonic sodium chloride such as 2% NaCl or ⅓ M sodium lactate solution, as emphasized by Dr. Berry.

It is disturbing that in spite of showing quite an interest in these problems, errors will occur on one's own service, and patients will be seen who have not been given sufficient electrolytes.

Another point that I should like to make is that whenever the extracellular fluid loss is more than 1,000 ml. a day (for example, drainage up to 2,000 or 3,000 ml. as by Wangensteen suction) then 24-hour replacement—that is, measuring what was lost one day and replacing it the next day—is insufficient. In such instances, replacement of what the patient is losing must be carried out every six hours. The surgeon should be quick to change the common routine to meet the needs of those with exceptional problems. He must also know where to find the information needed to help him handle such a case.

HEMOLYTIC REACTIONS ASSOCIATED WITH SURGICAL PROCEDURES

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AN INTEREST in the use of the artificial kidney has provided us with an opportunity for management of a number of patients with acute renal failure. In seven instances the acute renal failure followed intravascular hemolysis associated with a coincidental surgical procedure. This combination provides two important factors which portend a severe type of acute renal failure. Management of these seven patients has included conservative methods of fluid restriction and rigid electrolyte management. In two instances replacement transfusions were done 8 and 16 hours following the hemolytic reaction, and surgery was performed in an effort to remove the products of intravascular hemolysis. Dialysis with the artificial kidney was undertaken in four patients as an adjunct to conservative management. This report is concerned with the experience with these seven patients with hemolytic reactions associated with surgical procedures.

PHASES OF RENAL FAILURE

There are three phases of renal failure following a hemolytic reaction associated with surgery of which a thorough understanding is necessary for appropriate therapy. The course of events may be considered under the following categories—the reaction of shock phase, the phase of renal insufficiency, and the salt-losing diuresis.[1]

Intravascular hemolysis may be first manifested by shock, with a violent onset of chills, fever, and subjective complaints in the conscious patient. With the patient under general anesthesia hemolytic reactions may evoke no perceptible response. A hemorrhagic state during or following an incompatible transfusion reaction has been observed in some instances, manifested by uncontrollable bleeding at operation or during the early postoperative period. The management of this initial phase

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1. Muirhead, E. E.; Haley, A. E.; Haberman, S., and Hill, J. M.: Acute Renal Insufficiency Due to Incompatible Transfusion and Other Causes, with Particular Emphasis on Management, Blood, Spec. Issue No. 2, pp. 101-138, 1948.

should include measures directed toward sustaining an effective blood volume by replacing promptly the blood loss of surgery or parturition and treating the anemia resulting from the hemolysis.

The second phase of renal suppression is manifested by oliguria and anuria. In a series of 28 patients with major reactions reported on by Muirhead [2] acute renal failure developed in 24, 2 died in shock, and there were only 2 with hemoglobinuria without renal failure. This confirms the reported high incidence of renal failure following major hemolytic reactions. The oliguria and anuria may last for 8 to 12 days, after which a period of diuresis may occur. The azotemia is accompanied by a disturbance in electrolyte composition of the plasma, with acidosis primarily resulting from mounting organic salts, sulfates, and phosphates.

TABLE 1.—*Summary of Seven Patients with Hemolytic Reactions Associated with Surgery*

Case	Age, Yr.	Sex	Background of Hemolytic Reaction	Duration of Oliguria or Anuria, Days	Management	Comment
1*	35	F	Intra-abdominal hemorrhage; excision of tubovarian mass; transfusion 500 cc. (Type A B to O)	0	Replacement transfusion 1 vol.	Recovery; discharged 9 days
2	33	F	Dilation and curettage, uterine pack; transfusion 1,200 cc. (Type A to O)	0	Replacement transfusion 1 vol.	Recovery; discharged 9 days
3	25	F	Manual extraction of placenta; transfusion 500 cc; CDE (Rh) incompatibility	12	Artificial kidney dialysis (2 ×)	Recovery
4	33	F	Spontaneous miscarriage; manual extraction of placenta; serum hemoglobin 1,680 mg. per 100 cc.; ? cause of hemolysis	21	Artificial kidney dialysis (2 ×)	Recovery
5	36	F	Hysterectomy; hemolytic reaction ? cause; serum hemoglobin 9.9 mg. per 100 cc. (8th day)	10	Artificial kidney dialysis (1 ×)	Died, 20 days
6	54	M	Gastrectomy for ulcer; incompatible transfusion 1,500 cc. (Type A to O)	5	Conservative	Died, 5 days
7	38	F	Caesarean section; abruptio placenta; incompatible transfusion 500 cc. (Type A to O)	11	Conservative	Died, 11 days

* This case was previously reported.[3]

Successful management during the low urinary output phase depends upon diligent attention to the fluid and electrolyte composition of the blood. Water must be restricted to the actual amount of insensible water lost from the lungs and skin, which can be replaced by about 800 cc. daily, plus the water contained in urine and stool. The diet should be high in calories to minimize protein catabolism [3] but should contain as little potassium and sodium as practicable, since the anuric patient has no way of eliminating these substances. Alkalies are contraindicated. Acidosis is less harmful and more easily managed. With mounting azotemia the serum calcium falls and a progressive anemia may appear; consequently, benefit may be obtained by the administration of calcium gluconate parenterally and by the correc-

2. Muirhead, E. E.: Incompatible Blood Transfusions with Emphasis on Acute Renal Failure, Surg., Gynec. & Obst. **92**:734-746, 1951.

3. Conley, J. E.; Erbes, J.; Stoddard, F. J., and Frye, J.: Replacement Transfusion Following Administration of Incompatible Blood, Am. J. Clin. Path. **19**:1131-1134, 1949.

tion of anemia with red cell mass. In an occasional case, mounting azotemia and the worsening of the clinical condition of the patient may warrant consideration of some form of artificial dialysis if facilities are available.

REPORT OF CASES

CASE 2.—A 33-year-old housewife was admitted on Aug. 25, 1952, with a spontaneous abortion in the third month of her fourth pregnancy. Vaginal bleeding and abdominal cramps had begun six hours before admission. After admission bleeding per vaginam was copious, with blood clots but no fetal or placental tissue. On admission the patient was conscious but restless. The blood pressure was 90/60; pulse rate, 120. The extremities were cool and moist. Plasma, 250 cc., was given immediately, followed by 500 cc. of Type A, Rh-positive blood on the assumption that her blood was Type A, Rh positive. After 200 cc. was administered, the patient had a chill, with temperature 101 F., pulse rate 98, and respiration rate 32. There was nausea and an episode of vomiting. The blood pressure was 80/62. The first transfusion of blood was discontinued and a second transfusion of 500 cc. was begun and was administered without reaction. A third transfusion of 500 cc. of Type A blood was given, making a total of 1,200 cc. of blood. The blood pressure was 132/82, pulse rate 90, and respiration rate 28 at the completion of the transfusions.

The patient was transferred to the operating room and with use of general ether anesthesia a uterine curettage was performed, with removal of retained tissue. A uterine pack was inserted. During the preparation for surgery, catheterization of the urinary bladder yielded 50 cc. of dark bloody urine. A recheck of the patient's blood type showed her blood to be Type O, Rh positive. The urine hemoglobin was 1,500 mg. per 100 cc. and serum hemoglobin, 228 mg. per 100 cc.

A replacement transfusion of 6,000 cc. of Type O, Rh-positive low-isoagglutinin-titer blood was done eight hours after the beginning of the administration of the incompatible transfusions. The procedure required about two hours, with the radial artery used for exsanguination and both long saphenous veins used for simultaneous rapid administration. Thiopental (Pentothal) sodium anesthesia was used because of pain in legs along the distribution of long saphenous veins, associated with administration of the blood with pressure.

The urinary output for the eight hours prior to replacement transfusion was 150 cc., and this urine had been deep red and contained 1,100 mg. of albumin and 1,500 mg. of hemoglobin per 100 cc. During the 12 hours following replacement transfusion the urine output was 1,200 cc. For the remainder of the patient's hospital stay the urine output varied between 800 and 1,400 cc. daily. No hemoglobin was present in the urine 36 hours after the replacement transfusion (Table 2; Fig. 1). The patient was discharged home on the ninth postoperative day. Renal studies performed one month following discharge from the hospital revealed specific gravity of 1.022, urea clearance 98.4%, and phenolsulfonphthalein excretion of 40% in 15 minutes.

Comment.—Cases 1 and 2 are instances in which it appears that complete renal suppression was averted by replacement transfusion performed 8 hours and 16 hours after the administration of incompatible blood. The incidence of this mishap has been about 1 in every 2,750 transfusions during the past five years, which compares favorably with the reported incidence.[1] The administration of 1,200 cc. of Type AB blood to a patient with blood Type O should have resulted in an acute renal failure, especially when it was associated with a surgical procedure. In neither of these cases did renal failure develop. Kidney function showed no impairment.

CASE 5.—A 36-year-old housewife was admitted in the sixth month of her pregnancy to a hospital outside the city on May 16, 1952. Massive bleeding per vaginam began several hours before admission. The patient proceeded to have a miscarriage, and massive bleeding continued which was uncontrolled by uterine packing; consequently, a hysterectomy was performed. The convalescence was stormy, but the blood pressure was sustained above 100 mm. Hg systolic throughout. The patient had received 3,500 cc. of blood in about 24 hours. During the four days following surgery, the urine output fell from 600 to 70 cc. daily with rising levels of nonprotein nitrogen and creatinine. The patient was transferred to Columbia Hospital for consideration for dialysis on May 21, 1952.

On admission the patient was pale and lethargic and the sclerae were slightly icteric. The blood pressure was 110/72, pulse rate 110, and respiration rate 40. Rales were present at both lung bases. There was no sacral or ankle edema. The abdominal wound was edematous, and a serosanguineous exudate oozed from the incision.

Laboratory studies revealed a red blood cell count of 2,000,000, hemoglobin content 5.7 gm. per 100 cc., nonprotein nitrogen 216 mg. per 100 cc., creatinine 12.8 mg. per 100 cc., potassium 5.6 mEq. per liter, chlorides 86.7 mEq. per liter, and serum hemoglobin 9.9 mg. per 100 cc.

After admission all fluids were withheld because of development of slight pulmonary edema and the established complete anuria. The anemia was corrected by administration of 2,500 cc.

TABLE 2.—*Pertinent Laboratory Data from Case 2**

	8-26-52 A. M.	8-26-52 P. M.	8-27-52	8-28-52	8-29-52	8-30-52	(Discharged) 9-4-52
Urine Hgb., mg./100 cc.	1,500	800	300	..	0	..	..
Serum Hgb., mg./100 cc.	228	148	138	..	7.7	..	..
Urine Alb., mg./100 cc.	1,100	...	800	0	0	0	..
Urine Color	Black	Red	Amber	Amber	Amber	Amber	..
NPN, mg./100 cc.	.....	...	53	..	48	35	..
Creatinine, mg./100 cc.	.....	...	1.3	..	1.0	1.0	..
Prothrombin, %	.....	...	34	..	..	85	..

* Replacement transfusion of 1 vol., performed on Aug. 26, 1952, was followed by a substantial drop in urine and in serum hemoglobin.

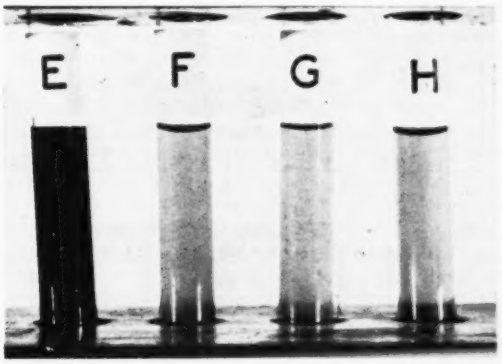

Fig. 1.—Note clearing of urine specimens in Case 2 following replacement transfusion of one volume. Urine specimen (*E*) obtained before replacement transfusion is compared with specimen (*F*) 4 hours, (*G*) 12 hours, and (*H*) 24 hours after transfusion.

of red cell mass. Because of mounting azotemia and coma with convulsions, artificial kidney dialysis was done for six hours on May 24, 1952.

On May 26, 1952, moderate diuresis commenced, with an output of 685 cc., which was low in sodium and chloride concentration. Thereafter urinary output varied from 1,000 to 2,500 cc. daily (Fig. 2). In spite of adequate urine output, after 11 days of oliguria and/or anuria, the patient's general condition worsened. Severe parotitis developed, with a continuous febrile course (temperature 101 to 103 F.). Serosanguineous exudate oozed copiously from the wound and per vaginam. The nonprotein nitrogen level remained over 250 mg. and the creatine level over 15 mg. per 100 cc., and the patient died on the 20th day after operation.

Autopsy showed significant gross changes in the pelvis and the kidneys. There was a granulating surface at the site of the cervical stump. A small retroperitoneal hemorrhage was present on the right pelvis. The kidneys were large and pale. Their aggregate weight was 500 gm. The capsules stripped with ease, leaving a smooth glistening pale brownish-gray surface. On section

the cortex bulged and was pale greenish-yellow. Differentiation between cortex and medulla was sharp. The cortex varied between 0.5 and 0.6 cm. in width and was traversed by faint radial reddish granular markings. Glomeruli were indistinct. The medullary pyramids were depressed and were a deep reddish-brown.

On microscopic examination the findings of greatest interest were in the pancreas, kidneys, and pituitary gland. The pancreas revealed dilatation and distention of acini and ducts by amorphous eosinophilic material. In some lobules these changes were of such intensity as to produce a pseudotubular appearance. The interstitial tissue were somewhat edematous. The islets were not remarkable.

The renal capsule was not thickened. The glomeruli were relatively normal, and there was no appreciable thickening of Bowman's capsule. Eosinophilic proteinaceous material was in the capsular space. The arterioles and interlobular arteries were relatively normal. The interstitial tissues were normal except about the distal convoluted tubules, where moderate increase in connective tissue was noted. The proximal and distal convoluted tubules exhibited varying degrees of repair and injury. In some the cells were necrotic and parts of the cells were lost into the lumen of the tubules. Nuclei of these cells were pyknotic or were fragmented. There were

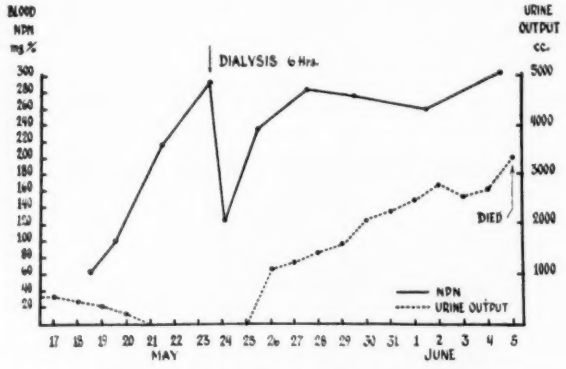

Fig. 2.—Nonprotein nitrogen and urine output in Case 5. There was a decrease in nonprotein nitrogen following artificial kidney dialysis for six hours, but "rebound" of nonprotein nitrogen promptly occurred.

many tubules in which the cells were flattened and the nuclei were hyperchromatic. Some of the tubules contained clumps of nuclear material mixed with albuminous fluid. In other tubules hyperplasia of the epithelium had occurred, and in still other places healing was almost complete. The cortical tubules contained occasional bile-stained hyaline casts, numerous heme casts, and occasional granular casts made up of desquamated epithelial cells and large phagocytes. In the medullary pyramids there was more intense congestion than in the cortex. The interstitial tissue was increased in amount. Many of the tubules contained coarse refractile brownish-green granules of hemosiderin pigment. This pigment was usually located along the periphery of the epithelial cells. Focal areas of infiltration of lymphocytes and plasma cells were also noted. More heme casts were present than in the cortex.

In the pituitary there was a rather extensive irregular area of infarction in the anterior lobe. There was fibrosis in this area associated with loss of staining reaction in the cells and the beginning invasion of the necrotic tissue by phagocytes. Occasional amyloid bodies and partially calcified round objects were noted. The non-necrotic portion of the lobe exhibited congestion, edema, and atrophy.

Comment.—Case 5 illustrates the progressive deterioration of a patient who had a hemolytic reaction associated with a surgical procedure. In spite of an adequate urinary output, complications developed and there was a fatal outcome. The cause

of the renal failure in this case is not clear, but the use of incompatible blood is a strong possibility. The temporary benefit of dialysis was nullified by the increased catabolism associated with continuous fever due to acute parotitis. Even the moderate diuresis which occurred during the last week of life resulted in no detectable reduction in the azotemia. The finding of necrosis in the anterior pituitary at autopsy suggests the possibility of secondary adrenal cortex failure in this case.

CASE 4.—A 33-year-old woman was hospitalized in another city on April 21, 1952, in the fifth month of pregnancy, because of a shaking chill of one and one-half hours' duration followed by a spontaneous abortion. When catheterization was done prior to manual removal of the placenta, approximately 100 cc. of black urine was obtained. There had been no subsequent voiding. The red blood cell count was 750,000, and the patient received a 2,000 cc. blood transfusion. She also received 500 cc. of 1/6 M sodium lactate solution and a rectal injection of sodium bicarbonate solution.

Previous drug therapy consisted of the administration of diethylstilbestrol throughout the pregnancy and, for two weeks prior to abortion, the use of penicillin and chloramphenicol for a vaginal infection. The patient has two children, aged 10 and 2 years. There had been three pregnancies in addition to the current one in the past 18 months, all terminating in spontaneous abortion during the first trimester. No other significant past medical history could be elicited.

The patient was transferred to Columbia Hospital on the second day of anuria. At this time the nonprotein nitrogen level was 124 mg. and the creatinine level 6.4 mg. per 100 cc. There was moderate acidosis, with CO_2 concentration of 13 mEq. per liter. The serum electrolyte levels were essentially normal. The serum hemoglobin was 1,680 mg. and the serum bilirubin was 6.8 mg. per 100 cc., 87% of which was the direct-reacting type. The whole blood hemoglobin was 11 gm., and the erythrocyte count was 3,560,000. Extensive investigation of the blood failed to reveal any immune or irregular isoantibodies. The acid fragility test was normal.

Treatment consisted of a diet which was limited to 35 gm. of protein and was low in potassium and sodium. The total fluid intake was limited to 750 cc. daily, including dietary liquids. Persistent nausea and vomiting kept the total caloric intake low. The pigment portion of the hemolyzed erythrocytes was excreted in the bile as evidenced by the numerous liquid, foul, black stools during the first two weeks of anuria. With this, the bilirubin concentration in the serum fell progressively to 2.0 mg. and 0.9 mg. per 100 cc. and the serum hemoglobin to 132 mg. and 7.1 mg. per 100 cc. on the fourth and eighth days respectively.

The clinical manifestations of uremia became progressively more serious after the seventh day. Extreme weakness, an "ammonia taste" in the mouth, and a urea odor to the breath were noted. Repeated emesis occurred, and pain in the anterior chest was accompanied by the appearance of a pericardial friction rub and right bundle-branch block, as interpreted from the electrocardiogram reading. Fluids were administered parenterally in the form of dextrose and distilled water to cover insensible and gastrointestinal losses. Although the concentration of electrolytes in the serum on the seventh day were sodium 132.5 mEq., chlorides 87 mEq. and CO_2 concentration 14 mEq. per liter, the administration of 1,000 cc. 1/6 M sodium lactate exerted no detectable beneficial effect. The subsequent appearance of dyspnea and precordial heaviness after the parenteral administration of fluid indicated that the lactate solution had merely expanded the extracellular compartment.

On the 12th day of anuria the situation was desperate. The patient was extremely restless and apprehensive, complaining of numbness and paresthesias of the extremities. Several mild convulsions occurred. Facial edema was noticeable but there was no edema of the sacrum or of the extremities. The maximum blood pressure was 120/64, with a pulse rate of 64. The nonprotein nitrogen of the blood was 296 mg. and the creatinine level 15.5 mg. per 100 cc. The serum potassium was 6.9 mEq., and the CO_2 was 13 mEq. per liter.

The patient's blood was dialyzed in the artificial kidney for a period of four and one-half hours on the 12th day, after which the nonprotein nitrogen of the blood was 180 mg. and the creatinine 11.4 mg. per 100 cc. The concentration of potassium in the serum had fallen to 5.2 mEq. per liter. After this, the patient's color was considerably improved; she was much more alert but remained very weak and listless. No further twitchings or convulsions were present.

Thirty-six hours after dialysis, chemical examination of the blood revealed a "rebound," with a nonprotein nitrogen level of 266 mg. and creatinine, 4.1 mg. per 100 cc. The patient remained anuric. (Fig. 3).

Difficulty was encountered in maintaining an accurate check of fluid and electrolyte intake and output because of recurrent vomiting and incontinence of feces. The concentration of serum sodium fell progressively. On the 17th day of anuria intravenous therapy was started. On the basis of the concentration of serum sodium of 122.5 mEq. per liter and a total body water of 35 liters (estimated weight 50 kg.), 500 cc. of 5% saline was administered without untoward effect. The concentration of sodium in the serum the next day was 137.5 mEq. and serum chlorides 96.8 mEq. per liter. In addition, the patient received on the 17th and 18th days of anuria, 1,000 cc. of blood, 2,000 cc. of 5% dextrose in saline, 50 cc. of calcium gluconate, and 200 cc. of dextrose in water, making a total of 3,250 cc. of liquid in 48 hours. This was given deliberately to correct a predicted extracellular fluid and electrolyte deficit. In spite of repeated examinations during the course of this therapy, pulmonary edema was precipitated without warning. The pulse rate rose to 120. Moist rales appeared in both lung fields, the abdomen became distended, the liver enlarged 4 fingerbreadths, and presacral edema appeared. Emergency treatment of this

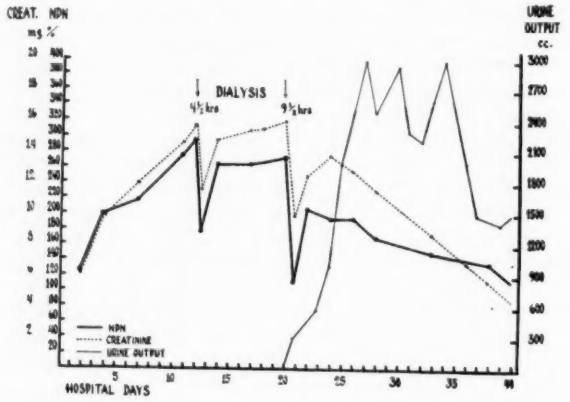

Fig. 3.—Urine output, serum nonprotein nitrogen levels, and creatinine course in Case 4. Note the "rebound" following artificial kidney dialysis on two occasions. The diuresis phase is shown after 21 days of anuria.

complication consisted of positive-pressure oxygen, the removal of 500 cc. of blood by phlebotomy, and the application of tourniquets to the extremities for a period of 12 hours. Anuria persisted.

On the 20th day spinal anesthesia to the level of the fourth thoracic vertebrae was maintained with 15 mg. of tetracaine (Pontocaine) hydrochloride for three hours without benefit. By the 21st day of anuria, azotemia was again extreme; the nonprotein nitrogen level was 272 mg. and the creatinine level 16 mg. per 100 cc., and the CO_2 was 13 mEq. per liter. It became technically impossible to determine concentrations of potassium because of excessive fibrin. The patient was acidotic, restless, apprehensive, confused, and delusional and at times appeared to have hallucinations. In desperation her blood was again dialyzed on the artificial kidney for nine and one-half hours. After dialysis the nonprotein nitrogen level was 112 mg. and the creatinine level 9.9 mg. per 100 cc., and the CO_2 was 22 mEq. per liter of serum.

Approximately 12 hours after this last dialysis, diuresis began, and 300 cc. of urine appeared per catheter during the first 24 hours. The volume of urine increased gradually over the next five days to 2,000 cc. daily, and this volume of urine was maintained daily thereafter. The "rebound" 36 hours after the second dialysis revealed the concentration of nonprotein nitrogen in the blood to be 206 mg. and creatinine 12.3 mg. per 100 cc. These values remained elevated for the next six days in spite of the diuresis and then gradually declined. Normal values of nonprotein nitrogen creatinine were observed for the first time 26 days after the onset of diuresis.

The patient was discharged from the hospital 36 days after her initial hemolytic episode. The nonprotein nitrogen level was 136 mg. and the creatinine level 5.7 mg. per 100 cc. Her mental status had improved, and, except for persistent weakness, lethargy, and nocturia, her condition had improved markedly.

Examination four months later revealed that persistent nocturia, with voiding two or three times a night, was still present. The maximum concentration power in the urine was 1.016, and the phenolsulphonphthalein excretion was 50% in 30 minutes. When seen for the six-month follow-up, all urinary symptoms had disappeared. The urea clearance test was 74% of normal. Examination at the end of nine months revealed no abnormal symptoms or signs. The blood pressure was 126/76. The ocular fundi were normal. A concentration test of the urine revealed a specific gravity of 1.025, with no reaction for albumin. Fifteen minutes after the injection of phenolsulphonphthalein, 90 cc. of urine containing 30% of the dye was collected. The urea clearance was 73% of average normal.

Comment.—This case is one of acute severe renal failure of 21 days' duration, which we feel would have terminated fatally except for the relief by artificial dialysis. The danger of overloading the circulation with water and electrolytes, even when there appears to be a need for them, was demonstrated. The final complete recovery as determined by tests of renal function is encouraging.

COMMENT

A hemolytic reaction associated with a surgical procedure constitutes a major catastrophe. The surgeon cannot view the mishap with complacency and base the prognosis on the favorable reports cited for conservative management of acute renal failure.[4] The associated surgical trauma and anesthesia may assign the following renal failure to a type of reaction called by Muirhead[5] "acute progressive unrelenting renal failure." There are numerous factors relating to the surgical procedure, such as trauma, anesthesia, dehydration, blood loss, anoxia, and hypotension, which tend to worsen the situation.

Attempts to produce hemoglobinuric nephrosis experimentally in animals have been successful for the most part only with the production of a high level of hemoglobinemia or by the intravenous injection of hemoglobin or laked erythrocytes into animals suffering from shock, dehydration, or previously damaged kidneys.[6] In animals, plasma hemoglobin concentrations as high as 3,700 to 8,000 mg. per 100 cc. were required to produce renal failure.[6] Of great importance is the rate of destruction of the incompatible red blood cells and the rate of clearance of the hemoglobin. It is estimated that 10 to 40% of the hemoglobin is cleared by the kidneys and 60 to 90% is presumably removed by phagocytosis or another mechanism. Two important factors related to the kidneys in acute renal failure are anoxia and exposure of the kidney to a sufficiently high concentration of the products of intravascular hemolysis.[4a]

Transfusions are often administered more rapidly to the surgical patients. This would allow the administration of a larger amount of blood, resulting in a shocking hemolytic reaction which would hasten the rate of destruction of incompatible red blood cells. Anesthesia masks symptoms of a transfusion reaction. Surgical patients

4. (*a*) Peters, J. P.: Lower Nephron Nephrosis, M. Arts & Sc. **6**:101-108, 1952. (*b*) Muirhead and co-workers.[2]

5. Muirhead, E. E., and Stirman, J. A.: Acute Progressive Unrelenting Renal Failure: Manifestation of Severe Shock Associated with Upper and Lower Nephron Nephrosis, Surgery **32**:43-57, 1952.

6. O'Donnell, W. M.: Pathogenesis of Oliguria in Eclampsia, Abortion and Abruptio Placentae, Am. J. Obst. & Gynec. **61**:641-646, 1951.

may be somewhat dehydrated by the preoperative withholding of fluids and the fluids unreplaced during surgery. Anoxia of the kidney as a result of blood loss or hypotension attending the surgical procedure may impair the renal blood flow, providing a more vulnerable renal setting for intravascular hemolysis.

Our experience with these seven patients would suggest that a more aggressive attitude must be adopted in the management of hemolytic reactions associated with surgical procedures. The program should include the recommended "conservative" methods of fluid restriction during renal suppression, prevention of acidosis, and rigid electrolyte management. If the hemolytic reaction is evident and if complete renal suppression is not established, as evidenced by anuria, replacement transfusion may be indicated to decrease the concentration of the hemoglobinemia. The two cases reported (Cases 1 and 2) had 1 vol. blood replacements performed 8 and 16 hours following the hemolytic reactions. Complete renal suppression was probably averted in these cases. According to Weiner and Wexler,[7] 1 vol. of patient's blood injected replaces 63.2% of the patient's circulating blood. A replacement of 1½ vol. will exchange 77.7% of the patient's blood. In Cases 1 and 2 1 vol. exchanges were performed. Further experience with this treatment seems indicated during the early oliguric phase rather than as adjunct to the dialysis for the advanced stage of azotemia suggested by Bessis [8] and Dausset.[9] Replacement transfusion of one volume is a simple procedure and well tolerated if the blood replacement is maintained at equal pace with the exsanguination. A prompt lowering of the concentration of the products of intravascular hemolysis which such a procedure effects may avert complete renal suppression in a situation where acute renal failure is almost a certainty and the prognosis is a grave one.

The artificial kidney for dialysis may be a valuable adjunct to the conservative management of the azotemia or potassium intoxication after the eighth day of renal failure. Clinical judgement should dictate when, and if, dialysis should be employed. In general, our experience with the artificial kidney has not been entirely a gratifying one. Reversible kidney lesions offer the most promising field for use of dialysis. Cases 3 and 4 illustrated instances in which we have felt that the dialysis with the artificial kidney was a valuable adjunct to the successful outcome.

SUMMARY AND CONCLUSIONS

Intravascular hemolysis associated with a surgical procedure constitutes a major catastrophe which portends a guarded prognosis with current methods of conservative management.

The success reported with replacement transfusion in two cases which appears to have prevented complete renal suppression suggests that this method can be used if the hemolytic reaction is detected early.

Prompt and complete correction of the anemia to minimize kidney anoxia is recommended.

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7. Wiener, A. S., and Wexler, I. B.: The Use of Heparin When Performing Exchange Blood Transfusions in Newborn Infants, J. Lab. & Clin. Med. **31**:1016-1019, 1946.

8. Bessis, M.: The Use of Replacement Transfusion in Diseases Other Than Hemolytic Disease of the Newborn, Blood **4**:324-337, 1949.

9. Dausset, J.: Lower Nephron Nephrosis: Report of Treatment of 44 Patients by Repeated Replacement Transfusions, Arch. Int. Med. **85**:416-431, 1950.

In an occasional case artificial dialysis may be a valuable adjunct to conservative management of the acute renal failure which occurs after hemolytic reactions associated with surgical procedures.

Dr. Paul I. Hoxworth, Eden & Bethesda Aves., Cincinnati.

Dr. Wm. O. McQuiston, 334 Parkside Drive, Peoria 5, Ill.

DISCUSSION

Dr. Paul I. Hoxworth, Cincinnati: The mortality from reactions to hemolytic blood transfusion prior to the advent of exchange transfusion and artificial dialysis was approximately 45%, and it is to be assumed that as data are gathered from these newer methods of treating the accident there will be noted a shrinkage in this mortality figure.

Another matter of extreme importance is to prevent this condition from occurring. Through better management in the laboratory and better understanding of methods of safeguarding against errors in technique due to carelessness, these reactions may be minimized. However, because of human error, not only in the laboratory but among the interns, residents, and nurses, these reactions can never be eliminated, and there will always be some of these problems to deal with.

I should like to compliment Dr. Conley on his presentation of this subject. It was very timely.

In closing I should like to suggest one other very important method of reducing accidents of these kinds. I refer to the less free use of blood. Blood transfusion is being employed entirely too often. We are electing blood transfusions much too frequently for moderate deficiencies in hemoglobin and red blood cell counts, and for anticipated shock in surgery. Blood can be poison, and, if other liquids are employed and if iron is used to correct anemias prior to surgery in some cases and after surgery in many cases, these measures are preferable to the use of blood transfusions.

Dr. William O. McQuiston, Peoria, Ill.: A simple method of treatment that was not mentioned was the employment of high spinal anesthesia. We have used it, even on infants approximately a year of age who had complete anuria following hemolytic reactions.

Frequently this technique is used in treatment; other methods are not necessary. Consequently, we have had no experience with use of the artificial kidney.

Dr. James E. Conley, Milwaukee: I should have mentioned the fact that we did use high spinal anesthesia and splanchnic nerve blocks on the two patients, one with 12 days and the other with 21 days of anuria, but with no apparent affect from the block.

For the patient who had anuria for 21 days, spinal anesthesia was used on the 4th and 19th days, and the anesthesia was brought to the level of the second thoracic vertebra and maintained for six hours. We saw no appreciable change in the urine output, which was nil.

Dr. Francis D. Murphy and the Staff of the Milwaukee County Hospital gave permission for the inclusion of Cases 3 and 7.

DUODENAL ULCER TREATED BY SUBDIAPHRAGMATIC VAGUS RESECTION AND POSTERIOR GASTROENTEROSTOMY

Interim Report

STANLEY O. HOERR, M.D.
CLEVELAND

THE PRESENT report traces for another year the histories of patients with duodenal ulcer who had a subdiaphragmatic vagus resection with posterior gastroenterostomy between September, 1946, and April, 1949. During this period, other types of operation were being performed for duodenal ulcer, but after preliminary trial, vagus resection with gastroenterostomy became the dominating procedure. This series is consecutive for vagus resection with gastroenterostomy for duodenal ulcer.

The report is based upon a group of 146 patients, followed for a minimum of three years; 56 patients have been followed five years, 59 have been followed four years, and 31 have been followed three years. Eight patients could not be traced this year, with the result that the follow-up is 95% complete.

MATERIAL

During the period in question, about 13.5% of all patients with duodenal ulcer seen and treated at the Cleveland Clinic had some type of operation performed. The medical treatment of all the patients included in this study was regarded as a failure. Chart 1 gives both primary and secondary indications for operation for the 146 patients covered by this report. In about half the cases the principal reason for operation was intractable pain. In most of the remainder the chief indication was obstruction, and in about 10% the main reason was hemorrhage. However, it may be seen that many patients had two indications for surgery, in that there was a history of bleeding in 25 cases in which operation was performed for other reasons—intractable pain or obstruction. Of the 146 patients, the ulcer of 14 had in the past perforated. In two patients the ulcer lay very near the pylorus, and associated antral spasm seen in x-rays raised the question of gastric cancer.

Chart 2 shows the duration of symptoms in this group of patients. It may be seen that the overwhelming majority had suffered from their ulcers for many years and that the operation was not undertaken for "acute" ulcer, insufficient time having elapsed to reveal whether or not the usual medical therapy would control the symptoms.

Chart 3 gives the age and sex distribution. There is the expected preponderance of males, and it may be seen that about half the patients were under the age of 50 years. Since it has been stated that in older patients gastroenterostomy alone often

From the Cleveland Clinic Foundation and Frank E. Bunts Educational Institute.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 7, 1953.

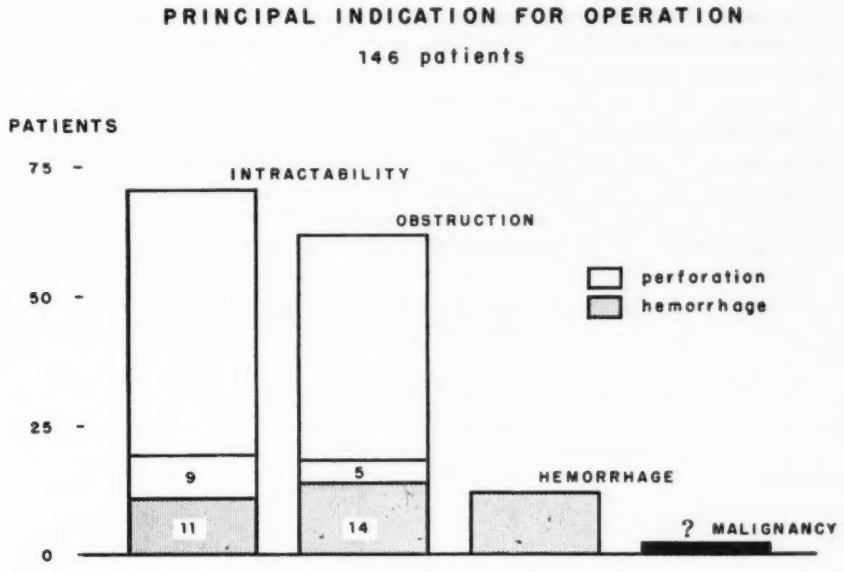

Chart 1.

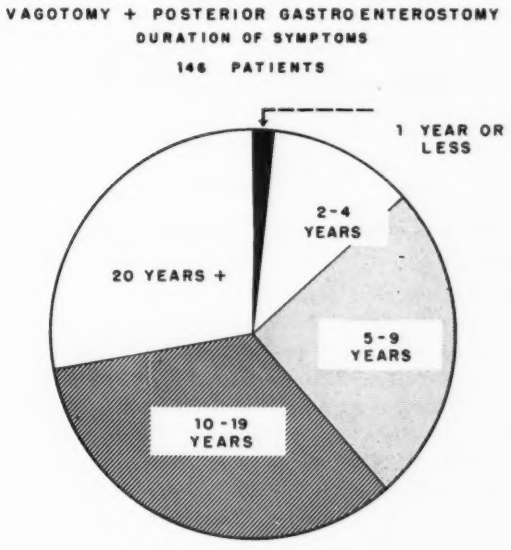

Chart 2.

suffices to control ulcer symptoms, it has a bearing to show that in this series there was a large group of younger patients, in whom gastroenterostomy alone could be expected to result in failure. Actually, in an analysis of failures, it will be shown that they occur in all age groups.

RESULTS

The follow-up on the 146 patients has in most instances been by means of questionnaire. While this method is open to objections, it does have the advantage of uniformity and forms a valid means of comparing one operation with another (i. e., gastric resection with vagus resection and gastroenterostomy). The questionnaire can establish accurately the patient's reaction to the operation and bring out

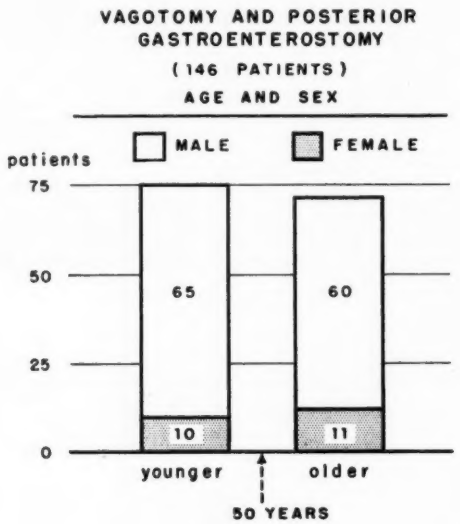

Chart 3.

such objective features as vomiting, serious hemorrhage, and inability to work. The questions asked are as follows:

1. Are you pursuing your usual occupation?
2. What is your present weight?
3. Has there been any ulcer type of pain since operation?
4. Do you have any other type of abdominal pain? If so, describe it.
5. Do you take any medicines regularly for your digestion?
6. Do you vomit? If so, how often?
7. Have you vomited blood or had tarry bowel movements?
8. How often do your bowels move?
9. Have you had any attacks of diarrhea? If so, how often?
10. Do you regularly have any unpleasant symtoms coming on during or right after any meal?
11. Do you regard yourself as entirely well?
12. Are you satisfied with the results of the operation?

Comments.

When the reply to the questionnaire indicated a poor clinical result, every effort was made to have the patient return for x-rays and further evaluation; in the few instances in which this was not possible, a follow-up report was obtained from other attending physicians.

The criteria employed in grading the results have remained strict. An "excellent" result means a patient asymptomatic as far as his gastrointestinal tract is concerned. He not only has no pain but follows no dietary restrictions. Ninety-nine patients (68%) qualified for this classification (Chart 4). A "good" result is one in which ulcer pain is not present but in which the patient may experience occasional bloating or vague abdominal distress. There is subjective satisfaction with the result of the operation; no medicine need be taken regularly, and the usual occupation is followed. Some of the patients are mildly neurotic and probably could never be completely well under any circumstances, and some undoubtedly have the irritable colon syn-

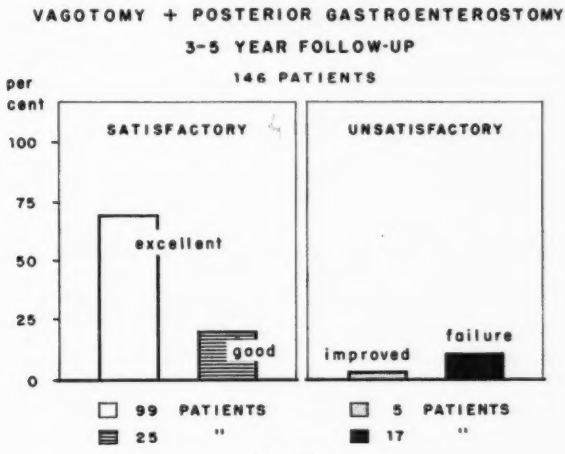

Chart 4.

drome. Twenty-five patients were placed in this classification (17%). The excellent and good results together produce a satisfactory clinical result, and in this follow-up study 85% of all the patients were grouped under this heading.

An "improved" patient is one who is still partly incapacitated from a gastrointestinal standpoint, but who does not give any history suggestive of true ulcer pain and who has no objective evidence of recurrent ulceration. Five patients were given this classification. Psychic factors seem to play a decisive role in qualifying a patient for this classification, but occasionally time proves that an organic lesion is present, as in one patient in whom a severe hemorrhage developed although no ulcer could be demonstrated by x-ray.

There are 17 clinical failures. In the previous report there were 10 recorded.[1] Eight patients have been added to the failure group since the last report, and one

1. Hoerr, S. O.; Brown, C. H.; Rumsey, E. W., and Crile, G., Jr.: Duodenal Ulcer: Results of Treatment with Subdiaphragmatic Vagus Resection and Gastroenterostomy; Interim Report, J. A. M. A. **149**:1437 (Aug. 16) 1952.

patient previously classed as having had a symptomatic failure, but who had no recurrent symptoms of ulcer and whose incapacitating troubles seemed largely psychological, improved sufficiently to be upgraded to the "improved" group. These 17 failures represent 12% of the entire group and, with the 5 patients listed as "improved," make up the 15% of those with unsatisfactory results.

Failures.—The reasons for the failures are given in Table 1. In seven instances the presence of ulcer was proved at a second operation; in four a probable jejunal ulcer was demonstrated by the x-rays; in three there was a sizable hemorrhage, and in three, although objective evidence of recurrent ulceration or hemorrhage was absent, gastrointestinal symptoms were of sufficient severity to interfere with a normal existence. In at least one of these three patients the symptoms do not suggest an ulcer but suggest a rather severe form of the "dump" syndrome.

TABLE 1.—*Causes of Failure of Vagotomy and Posterior Gastroenterostomy (One Hundred Forty-Six Patients)*

Cause of Failure	No. of Patients
Ulcer disclosed at 2d operation	7
Ulcer suggested by x-rays	4
Ulcer suggested by hemorrhage	3
Symptomatic failure only	3
Total failures	17 (12%)

TABLE 2.—*Time of Onset of Symptoms After Vagotomy and Posterior Gastroenterostomy (Seventeen Failures)*

Onset of Symptoms	No. of Patients
Immediately after operation	4
Within 2 years	5
Two years or more after operation	8

In Table 2 is found the time when troublesome symptoms first appeared after the operation. The fact that eight patients showed their first evidence of trouble more than two years after their operation is disturbing and accentuates the need for a long-term follow-up. In three of these the interval was more than three years. These long intervals account for the sharp upward jump in failures from 7% last year to 12% this year.

Table 3 gives the present status of the 17 failures. Three patients are dead, one as a direct result of his ulcer disease, having died of an operation at another hospital. The disease of eight is well controlled, either by reason of a subsequent resection or by means of a conservative ulcer regimen. One patient is still partly incapacitated after a secondary gastric resection. Three patients are suffering from poorly controlled ulcer symptoms, and in two patients who had a large hemorrhage without other significant complaint the result is unknown.

Attempts to relate the failures to some specific factor have not been very helpful. In two instances it was known that the vagotomy was incomplete by the demonstration of overlooked fibers at a second operation. In three instances it was ascer-

tained that the stoma was not functioning properly, the faulty function leading either to obstructive symptoms or to recurrent duodenal ulceration. In two cases of symptomatic failure with no proof of recurrent ulceration, there was scant evidence of a duodenal ulcer at the time of operation. But in 10 cases there was no suggestive reason for failure, from the standpoint either of technique or of selection. It is of interest that none of the 17 patients whose treatment failed happened to be females; this fact was undoubtedly purely accidental. The indication for surgery had no bearing; the indication in 10 cases had been intractability, in 6, obstruction (with which one would expect a good result from the gastroenterostomy alone), and in 1, hemorrhage. Age seemed to have no bearing, seven of the patients being over 50 years of age.

Postoperative Diarrhea.—This is the most difficult item on the questionnaire to evaluate, and it is, in my opinion, of limited significance. Infrequent or intermittent diarrhea, as reported by 22 patients, whether troublesome or mild, is probably unrelated to the operation. The condition of 12 patients who reported daily diarrhea is likewise difficult to evaluate; several reported that they had a single "loose" stool,

TABLE 3.—*Present Status of Seventeen Patients in Whom Treatment Failed*

		No. of Patients
Patient dead		3
Mesenteric thrombosis	1	
Bronchogenic carcinoma	1	
Secondary operation	1	
Resection performed		5
Satisfactory	4	
Unsatisfactory	1	
Controlled by dietary regimen		4
Uncontrolled		3
Unknown (1 hemorrhage each)		2

which cannot really be regarded as abnormal, or they had two or three normal bowel movements in a single day, a situation, again, within normal limits. Among the four patients who speak of daily troublesome diarrhea, there is at least one who had chronic diarrhea before he had his operation. It seems reasonable to conclude on the basis of these data that, irrespective of the ultimate relationship of vagus resection to diarrhea, in this series it has not proved to be a complication of any significance.

COMMENT

Although the increase in failures from 7 to 12% in the past year has been a disappointment, it should be noted that recurrent ulceration is actually proved in only 11 patients, or 8% (in 7 by operation and in 4 by x-rays). The apparent failure in the other 6 patients may ultimately prove to be due to some other cause. It had also been hoped that those patients who were going to have trouble would show symptoms within a year or two of operation. Even though all surgeons are aware of the occasional patient who remains symptom-free for years after a gastroenterostomy before he bleeds from an unsuspected jejunal ulcer, or has an acute perforation, such cases are exceptional. It may be that in a small series such as this one the sudden increase in failures in the past year lies entirely within the law of chance, and subsequent years will reveal only a sporadic new failure or none at all.

Two points should be borne in mind before too great a significance is attached to the increase in failures. The criteria employed in evaluating the results are strict, and when they are applied with equal severity to other operations, such as radical gastric resection, there is also a high failure rate from untoward symptoms due to the small remnant of stomach, and so on. Evidence that the criteria employed are strict may be obtained by implication from the recent report of the vagotomy committee.[2] The conclusion is drawn that vagus resection with gastroenterostomy is inferior to gastric resection in the surgical treatment of duodenal ulcer. Although time may prove the conclusion to be correct, there is no striking evidence given in the report to support such a conclusion. In fact, if an error in one table is corrected (it resulted from a simple transposition of figures), vagus resection with gastroenterostomy becomes the virtual equal of gastric resection in producing the important category of "clinical freedom from ulcer symptoms." In Table 4, I have taken the liberty of assembling data given in that report in such a way that vagus resection with gastroenterostomy seems to be the operation of choice for duodenal ulcer! The percentage of good results would seem to be entirely too optimistic for all the operations listed, including gastric resection. It is probably a result of a combination of easier criteria and too short a period of follow-up (less than three years). Note in this connection the low incidence of proved recurrent ulceration for all three procedures listed.

TABLE 4.—*Data Taken from Vagotomy Committee Report**

	I Clinical Freedom from Ulcer Symptoms	II Patient Able to Work	III Patient Satisfied with Operation	IV Hospital Mortality	V Recurrent Ulceration Disclosed by X-Ray
Gastric resection	95.7%	92.0%	93.5%	3.0%	1.7%
Vagotomy and gastric resection	96.6%	90.4%	96.1%	1.9%	1.4%
Vagotomy and posterior gastroenterostomy	94.5%	94.7%	93.8%	1.3%	2.7%

* Column I was taken from Table 3, page 463, and Table 26, page 335, as corrected; Column II, from Table 7, page 467; Column III, from Table 5, page 465; Column IV, from Table 17, page 480, and Column V, from Table 9, page 469.[2]

The second important point is that the patients reported on represent the first ones upon whom the operation was done. In the past three years, there have been changes in technique, particularly in the placement and construction of the gastroenterostomy,[3] which have cut down immediate postoperative morbidity to a significant degree. It is not impossible that these changes will have a bearing on the end-result as well.

At this phase of the study, one would be led to believe that the rate of recurrent ulceration following vagus resection with gastroenterostomy will prove to be greater than that following radical gastric resection. It also seems clear that a long-term follow-up will be necessary to settle the point. If the rate of recurrent ulceration actually does prove to be higher, in the end, should one assume that there is no place for the operation of vagus resection with gastroenterostomy? My colleagues and I are continuing to perform the operation in a selective way for two principal

2. Report of the Committee on Surgical Procedures of the National Committee on Peptic Ulcer of the American Gastroenterological Association, Gastroenterology **22**:295 (Nov.) 1952.

3. Crile, G., Jr.: Technique of Vagotomy and Gastroenterostomy in Treatment of Duodenal Ulcer, Surg., Gynec. & Obst. **92**:309 (March) 1951.

reasons: First, we cannot approach the mortality rate of 0.5% with unselective gastric resection; second, the patients who do well after this operation—the 85% with satisfactory results—impress one as being in perfect health almost from the time of surgery. After radical gastric resection, this is not so frequent a phenomenon, and in my experience there is often an adjustment period of many months before the patient can be regarded as perfectly normal, if he ever becomes so.

Therefore, my colleagues and I are convinced that the principle of vagus resection is sound and that the operation ideally should be performed upon every patient having surgery for a duodenal ulcer. It is amply proved that an additional procedure is essential; the selection of this procedure will vary with circumstances. It may be possible to preserve the low mortality rate of vagus resection with the low recurrence rate of gastric resection by combining vagus resection with a limited gastric resection (50%), as suggested by Colp and associates [4] and Smithwick and his colleagues,[5] and still avoid the disability of the "small stomach." It is, therefore, our present plan to perform a vagus resection with limited gastric resection on every patient on whom this can apparently be done without increasing the risk; i. e., on good-risk patients in whom the ulcer is not encroaching on the gastrohepatic ligament and its contained structures. On the poor-risk patient, or on the patient in whom the character of the ulcer greatly increases the hazard of a gastric resection, a vagus resection with gastroenterostomy is performed, in the belief that there is nearly a 90% chance that a good result will follow.

SUMMARY AND CONCLUSIONS

A continuing follow-up study on a group of patients who had a vagus resection with posterior gastroenterostomy three or more years ago discloses the fact that there are 85% of satisfactory clinical results and 12% of failures when strict criteria are employed. An increase in failures from 10 to 17 in this group of 146 patients is disappointing, but it is pointed out that recurrent ulceration has been "proved" by operation or x-rays in 11 (8%), and in the other 6 the failure may be due to other factors.

Even if a long-term follow-up discloses a higher rate of recurrent ulceration with this procedure than with radical gastric resection, my colleagues and I are convinced that the principle of vagus resection is sound and that this procedure should ideally be carried out on every patient requiring an operation for duodenal ulcer. Since an additional procedure is invariably needed, it may be that a limited gastric resection with vagus resection will prove to be the procedure of choice for good-risk patients and will preserve a low mortality, prevent the disability of the "small stomach," and still protect against a high rate of recurrent ulceration. On patients who are poor operative risks or in whom the nature of the ulcer markedly increases the hazard of a resection, a gastroenterostomy may be performed with the vagus resection, with the expectation of a satisfactory result in a high proportion of cases.

4. Druckerman, L. J.; Weinstein, V.; Klingenstein, P., and Colp, R.: Comparative Study of Subtotal Gastrectomy With and Without Infra-Diaphragmatic Vagotomy in Surgical Therapy of Duodenal Ulcer, Ann. Surg. **136**:211 (Aug.) 1952.

5. Farmer, D. A.; Howe, C. W.; Porrell, W. J., and Smithwick, R. H.: Effect of Various Surgical Procedures upon Acidity of Gastric Contents of Ulcer Patients, Ann. Surg. **134**:319 (Sept.) 1951.

TREATMENT OF DUODENAL ULCER BY SUBTOTAL GASTRIC RESECTION

A Ten-Year Study

OWEN G. McDONALD, M.D.
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AND
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PROGRESS in medicine is directly related to the willingness of the profession to apply and evaluate new forms of therapy. Surgeons were encouraged when Dragstedt [1] advocated and performed vagus section for the treatment of duodenal ulcer. Gastroenterostomy and pyloroplasty had proved inadequate, and gastric resection was followed by a substantial mortality and morbidity. Because of the high percentage of major complications, such as marginal ulcer, obstruction at the site of anastamosis, and leakage from the duodenal stump, American surgeons were slow to accept gastric resection. At the Duluth Clinic, it was not until 1938 that the number of resections exceeded the total figure for gastroenterostomy and pyloroplasty. Although some surgeons and medical centers preceded us in this transition, others followed by a number of years.

We have rarely used vagus resection in treating duodenal ulcer because of our satisfaction with subtotal gastric resection. This is a review of our experience with gastrectomy and includes all operations performed since vagotomy was introduced, in 1943.

The short-term results in those patients who underwent resection between 1943 and 1947 were reported previously to the Central Surgical Association by La Bree and Gillespie.[2] That group has been restudied to ascertain long-term results, and, in addition, we are reporting on those resections carried out during the past five years.

In 93 patients, who underwent resection five to nine years ago for benign duodenal ulcer, there were six postoperative deaths and six unrelated deaths three or more years after operation. Sixty-eight patients returned for examination or answered our questionnaire. In this follow-up study, the following facts were noted:

1. The one patient who suffered hemorrhage five weeks after surgery has had no bleeding during the seven years since.
2. No patient had clinical evidence of an ulcer, and of 23 studied by x-rays none had evidence of a recurrent or marginal ulcer.

From the Department of Surgery, Duluth Clinic, Duluth, Minn.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 7, 1953.

1. Dragstedt, L. R., and Owens, F. M., Jr.: Proc. Soc. Exper. Biol. & Med. **53**:152-154 (June) 1943.

2. LaBree, R. H., and Gillespie, M. G.: Arch. Surg. **59**:750-757 (Sept.) 1949.

3. Sixty (88%) had maintained or increased their weight.
4. Of 40 patients tested, 37 (90%) still had a histamine achlorhydria.
5. Sixty-four (94%) resumed their preoperative duties. Four said they were unable to continue in their former occupation, but all were gainfully employed.
6. Previously reported symptoms of hypoglycemia (the dumping syndrome) are now absent in two patients but in one they persist.
7. A small number of patients reported an intolerance to such food items as spices, fat, milk, coffee, and chocolate.

In tabulating the data on long-term results, we accepted the evaluation as given by the patient with a single exception—the one with hypoglycemia. His result was graded down from good to poor. Five or more years after operation, then, 60 (88%) of the patients had a good or excellent result and 8 (12%) were not entirely satisfied with the operation.[3] Most of the unsatisfactory results occurred in patients in whom persistent pain was the only indication for operation.

A separate study was made of the 141 patients who had a subtotal gastric resection for duodenal ulcer during the past five years. The Department of Internal

TABLE 1.—*Previous Operations*

Type of Operation	1943-1947 93 Patients	1948-1952 141 Patients
Perforation (acute)	13	12
Gastroenterostomy	5	2
Pyloroplasty	4	4
Exploratory	2	0
Gastric resection	2	0
Vagotomy	1	1
Total	27 (30%)	19 (13%)

Medicine supervised the treatment of every patient, and we believe all had a fair trial on medical therapy. The average duration of symptoms before surgery was 11 years. The age of patients, the sex distribution, and the indications for operation have not changed appreciably. However, the following factors may have influenced results in this second series:

1. More extensive resection
2. Fewer previous operations
3. Antibiotics and blood transfusions
4. Improved anesthesia
5. Standardization of surgical procedure

Our resection was increased to include 75% of the stomach, especially where acid values were high. However, in the small percentage of patients in whom resection was done primarily for obstruction, who had low acid values, and especially those whose occupation required considerable physical labor, we were content with a two-thirds resection. We prefer a Hofmeister short-loop posterior gastrojejunostomy but utilize other standard procedures whenever an indication arises. In contrast to

3. The remaining 13 patients, all of whom reported a good or excellent result four years ago, are not included in these statistics.

the earlier group, here it was less common to encounter a patient who had had previous surgical treatment for a peptic ulcer except for closure of an acute perforation.

There has been a gratifying reduction in postoperative complications.

We think that improved tracheal toilet during and after anesthesia has been an important factor in reducing pulmonary complications. One blown-out stump occurred in a patient with a difficult duodenal closure. Although many surgeons insert a tube into the distal loop for feeding purposes, we prefer to decompress the proximal loop and protect the stump closure. Our tube has additional openings for gastric suction. Delayed emptying occurred in two patients but had corrected itself spontaneously by the time the patients left the hospital on the 11th and 12th days, respectively. In one patient bleeding occurred on the third postoperative day. Undoubtedly it was due to an error in surgical technique, because the ulcer had been removed. No patient has required secondary operation for a malfunctioning stoma.

TABLE 2.—*Postoperative Complications*

Type	1943-1947 93 Patients	1948-1952 141 Patients
Pulmonary	5	2
Infections	8	2
Duodenal leak	1	1
Retention	2	2
Hemorrhage	2	1
Intestinal obstruction	1	0
Wound separation	1	1
Total	20 (21%)	9 (6%)

Of the 141 patients, 132 cooperated in this study. In evaluating results reference was made to the following criteria:

1. Recurrent ulcer or late hemorrhage
2. Influence on weight
3. Postoperative acidity
4. Ability to perform usual duties
5. Food intolerance
6. Patients' evaluation of the result

Sixty patients had x-ray examinations. There was one marginal ulcer and one recurrent duodenal ulcer, the latter in a patient who had a Billroth-I procedure. No patient has offered evidence of late hemorrhage.

If we may accept a 5 lb. (2.3 kg.) weight variation as the equal of the patient's preoperative weight, then 105 (80%) maintained or increased their weight. For the 27 (20%) who had lost weight, the average loss was 14 lb. (6.4 kg.).

Acid values were determined on 83 patients. Seventy-five (90%) were free of acid after histamine and 8 (10%) had an average of 20 units of free acid.

One hundred and twenty-two patients (92%) have returned to their former occupation. Four were limited by physical disabilities unrelated to the operation. Six patients found it necessary to change to less strenuous duties, but all were gainfully employed. Intolerance to specific food items was the same as described for the previous group. There are two patients with hypoglycemia (the dumping syndrome). The average hemoglobin value for the series was 88%.

In this group of 141 patients who had subtotal gastric resection for duodenal ulcer, there has been no mortality.

During the same interval, we have carried out 275 consecutive subtotal gastric resections for benign duodenal, gastric, and gastrojejunal ulcer, including those operations for uncontrolled bleeding, with but one death.

Again, patients were asked to evaluate the operation as it affected them. One hundred and twenty-two (92%) reported excellent and good results. Five (4%) said the result was fair and five (4%) said it was poor.

CONCLUSIONS

1. Subtotal gastric resection is an eminently safe surgical procedure and produces good to excellent results in approximately 90% of cases.
2. Disabling sequelae are rare.
3. The great majority of patients adjust well to gastric resection.

TABLE 3.—*Mortality in All Subtotal Gastric Resections, 1948-1952*

Site of Ulcer	No.	Deaths
Duodenal	141	0
Gastric or marginal	134	1 (0.7%)
Total	275	1 (0.35%)

TABLE 4.—*Results of Subtotal Gastric Resection for Duodenal Ulcer, 1948-1952*

Result	No.	%
Excellent or good	122	92
Fair	5	4
Poor	5	4
Total	132	100

DISCUSSION

ON PAPERS BY DR. HOERR AND DRS. MC DONALD, LA BREE, AND GILLESPIE

DR. EDWIN M. MILLER, Chicago: Certainly nothing but praise could be said in the discussion of Dr. McDonald's rather remarkable series of results with gastric resection.

He stated, I believe, that in the beginning they were rather dissatisfied with their experiences with vagotomy, but I don't believe he stated the reasons for this dissatisfaction.

Personally, I believe that every man should have an open mind when he is dealing with these problems. I am one of those who feel that gastric resection, as it is done today, is in most instances a satisfactory operation, but I also believe that Dr. Dragstedt has made a very valuable contribution.

I am one of those who have seen fit, up to now, to do a fair number of vagus nerve resections with gastroenterostomy, but I still feel that the decision between resection or vagotomy not only must be made in the careful preoperative study of the clinical picture, but must be made with the abdomen open, and with a very thorough evaluation of the extent of the pathology, because there are some situations in which one would hesitate very much about proceeding with a resection, even though he had anticipated doing so. The extent of the pathology of the duodenum, the extent of the scar tissue, the extent of the edema down toward the common duct would make it rather hazardous in many instances, I believe, to proceed with the resection. In those cases

I certainly would not hesitate to change my mind immediately, and to proceed with a vagotomy and gastroenterostomy. After all, safety is the principal consideration.

I also think that if we select our cases very carefully, we shall find preoperatively that some patients who respond positively to the insulin test will show evidence that most of the acid is secreted through the stimulation of the vagi. Especially is this so in the younger group of individuals who are of nervous temperament and who have very high acid values. I believe that to this type of patient, vagotomy with gastroenterostomy is better suited than a resection.

But I would certainly congratulate Dr. McDonald and his group. I think that this is a remarkable series. A careful follow-up with so few postoperative complications and such a low mortality rate is indeed very gratifying, and I can see they had little need for an alternative procedure, such as vagotomy.

I was also interested in Dr. Hoerr's remarks about their combination, lately, of vagotomy with a more or less radical resection. I should be very much interested to see how the results in that series of patients compares with the results in those who have had a vagotomy and gastroenterostomy alone, and in those that have had a high resection alone.

Dr. Henry K. Ransom, Ann Arbor, Mich: I, too, would like to congratulate Dr. McDonald on this very excellent series of cases that he has reported. I would also like to comment briefly on Dr. Hoerr's paper, because his results and his ideas are quite similar to ours (Pollard, H. M.; Bolt, R. J.; Ransom, H. K., and Orebaugh, J. E.: Comparison of Results of Vagotomy and Subtotal Gastrectomy for Duodenal Ulcer, *J. A. M. A.* **150**:1476. 1952).

Last year we assembled data concerning 38 patients who had been treated by vagotomy during the years 1946 and 1947, and who, therefore, were suitable for a five-year evaluation of results.

Twelve patients were treated by vagotomy alone; 21 were treated by vagotomy plus gastroenterostomy or pyloroplasty; 3 were treated by vagotomy combined with gastric resection. All these operations were performed in cases of chronic duodenal ulcer. In two cases, vagotomy alone was employed in the treatment of marginal ulcer which developed after gastroenterostomy for duodenal ulcer.

There were no operative deaths. When the entire group was considered, 34 patients, or 89.5% were regarded as having satisfactory results at the end of the first year, whereas in only 29 cases, 78.4%, were the results rated as satisfactory at the end of the second year. The results at the end of the fifth year were identical with those noted at the end of the second year.

When vagotomy alone was considered [slide], the number of satisfactory results at the end of the first year was 83.4%, but only 63.6% at the end of the second year. Again, results at the end of the fifth year were the same.

Patients treated by vagotomy plus gastric drainage operations showed the highest incidence of good results: In this group 90.5% had satisfactory results at the end of the first year, whereas at the end of the second and fifth years 85.7% were listed as satisfactory.

In other words, our experience has been a little different from Dr. Hoerr's, because we found that the status at the end of the second year and that at the end of the fifth year were identical, but this is a small series, and, of course, is open to the criticism of evaluation of any small group of patients.

In spite of the fact that the results in this small group of cases compare favorably with those of any other surgical procedures, we have been hesitant to adopt vagotomy and gastroenterostomy as a routine form of treatment until more time has passed and more cases are available for appraisal.

Without question, the comparative safety of this procedure will make it a valuable expedient for elderly or poor-risk patients, and for those in whom the technical problems of a difficult dissection or an insecure closure of the duodenal stump would make subtotal gastrectomy a hazardous undertaking.

Moreover, even though a low operative mortality and low recurrence rates are reported by many authors for subtotal gastrectomy, this is not an ideal procedure, since 10 to 15% of the patients have distressing side-effects following the operation. These range from the dumping

syndrome and the hypoglycemic syndrome to severe nutritional disorders characterized by gradual but often marked weight loss, weakness, and general debility—a condition quite refractory to treatment.

For this reason we have recently adopted the procedure recommended by Farmer and others (Farmer, D. A.; Howe, C. W.; Porell, W. J., and Smithwick, R. H.: Effect of Various Surgical Procedures upon Acidity of Gastric Contents of Ulcer Patients, *Ann. Surg.* **134**:319, 1951), that is, hemigastrectomy, or a 50% resection, combined with bilateral subdiaphragmatic vagotomy. Theoretically, by leaving a larger gastric pouch, some of these physiologic and metabolic problems may be eliminated. In addition, this combined procedure seems to be the logical approach to the ulcer diathesis, since it attacks the cephalic as well as the hormonal phases of gastric resection. Whether the incidence of recurrent ulcer will be higher than with the conventional three-quarters resection remains to be seen.

DR. LOUIS T. PALUMBO, Des Moines, Iowa: These were two excellent presentations.

Before 1947, we were employing a partial gastrectomy which removed 75% of the stomach, the prepyloric area, and the first part of the duodenum, including the ulcer, in practically all of our cases.

In 1947 we embarked on another program, in which we combined infradiaphragmatic vagus resection with partial gastrectomy, in about 43 patients, unselected and consecutive. Our thought at that time was that possibly, by combining both procedures, we might produce a persistent achlorhydria and eliminate marginal ulcer, and that with the delayed emptying of the gastric remnant we might eliminate the dumping syndrome. Also, at some future date, if the results of this combined procedure were favorable, a less radical gastrectomy might be performed.

We have followed these patients very carefully, and since 1949 we have gone back to our partial gastrectomy as the operation of choice in practically all of our cases. We have about 300 in the partial gastrectomy group, and 43 in the other group.

We use the combined operation at the present time only in those patients who are the high-tensive, emotional type, who have a high night gastric secretion volume and a high response following the insulin test. In a careful survey over a period of five to six years in this group, we feel that the over-all results in the combined group are more unsatisfactory than in our partial gastrectomy group alone.

We have had no marginal ulcers to date in the combined operation. We have performed thorough gastric studies, and in the partial gastrectomy group alone we have had 91% achlorhydria on the fasting specimen, but after histamine 31% showed free acids.

In the combined group, when the vagus resection has been done with partial gastrectomy, we have had 100% achlorhydria, which has persisted four to six years, and even after insulin we have had no free acid in these patients. The incidence of the dumping syndrome has remained the same in both groups.

We have also performed thorough motor meal studies of the small bowel and colon on these groups, and we find that in the combined procedure, in about one-third of the patients studied, segmentation, clumping, and puddling of barium in the terminal ileum occurs. This has persisted in these cases for three to six years without any changes, and there has also been hypomotility of the small bowel in this group. The average emptying time has been about six hours. These changes, however, to date have caused no physiological disturbances to affect the health of the individual beyond that of the other patients in this series who did not show these changes.

I would like to ask Dr. Hoerr if he has done any of these studies, and if he has had 100% persistent achlorhydria after insulin.

DR. STANLEY O. HOERR, Cleveland: I should like to thank Dr. Miller, Dr. Ransom, and Dr. Palumbo for their comments, and I should like to join in their congratulations to Dr. McDonald and his colleagues for the excellent results that they have had with gastric resection.

In answer to Dr. Palumbo's question, I'm sorry to say that we do not have detailed physiological postoperative studies on our patients, since about three-quarters of them come from considerable distances away, and it is impractical to bring them back if they are asymptomatic.

I should like to give as my own conviction that the ultimate place of vagus resection—with or without other assorted procedures—is not going to be settled today, and is probably not

going to be settled for some years to come, but I note that even with the skillful surgery which Dr. McDonald and his colleagues performed, there were occasional instances when they shied clear from gastric resection and performed lesser procedures, like gastroenterostomy.

Irrespective of the ultimate place of the operation, I believe it is worth considering when one comes up against a patient in whom a gastric resection is going to be extremely difficult. Under such circumstances, I think we have enough evidence to warrant us (even those of you who shudder and turn pale at the thought of a vagus resection) in performing a vagus resection with gastroenterostomy, with a clear conscience.

DR. OWEN G. MCDONALD, Duluth, Minn.: I, too, would like to thank Drs. Ransom, Palumbo, and Miller for their kind comments.

Dr. Miller, possibly our attitude regarding vagotomy was not stated clearly. We have not utilized the procedure enough to evaluate results, simply because we have been so pleased with subtotal resection.

I am sure all will be interested in the long-term results provided by any operation which combines a lesser resection with vagotomy.

SURGICAL TREATMENT OF GIANT-SIZED BENIGN PENETRATING ULCERS OF THE STOMACH

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AND
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ST. LOUIS

THE PURPOSES of this presentation are to discuss certain unusual aspects of benign gastric ulcers and to examine the surgical approach to these lesions. The ulcers under consideration are huge, measuring over 6 cm. in at least one diameter, and they have been proved benign by histologic study. Also, they are penetrating in that the entire thickness of the gastric wall over a large area has been destroyed—the defect being filled by some adjacent organ.

REPORT OF CASES

CASE 1.—C. D., a white man, aged 55, had had symptoms of nagging pains in the epigastrium for seven months, with no anorexia, weight loss, nausea, or vomiting. Three months prior to admission he had nausea, vomiting, fullness in the stomach, anorexia, weight loss, but no blood in either vomitus or stool. During two months prior to admission he began to notice weakness and a weight loss which totaled 25 lb. (11.3 kg.) at the time of admission. There was a history of a cerebrovascular accident prior to admission.

On admission to Barnes Hospital he had marked epigastric tenderness, but no masses were palpable. The guaiac test of the gastric contents was positive. On x-ray examination there was a large ulcer of the lesser curvature. This suggested lymphosarcoma of the stomach to the radiologists. On gastroscopy a large ulcerating lesion was seen extending from the antrum to the cardia, described as "a white infiltrating neoplastic lesion with deep ulceration and with stiffening of the adjacent wall." No diagnosis could be made from the gastric washings. There was no anemia.

At operation on Sept. 19, 1951, a huge ulcer occupying almost the entire posterior aspect of the stomach adherent to the transverse mesocolon, gastrohepatic ligament, and pancreas was discovered. Biopsy specimens were taken which were interpreted as benign by frozen section. The stomach was freed from the edge of the ulcer which measured 7 cm. in diameter. The pancreas buttressed the wall of the stomach which was entirely lacking throughout the area of ulceration. The ulcer bed was left intact on the pancreas and the hole in the stomach closed. Because of the patient's poor condition, a resection was deemed inadvisable at that time. Induration of the area posterior to the stomach extended from the pancreas up toward the esophagus. No drainage was employed. Through the abdominal incision a pancreatic fistula developed. This closed spontaneously, and the patient was discharged in good condition. He died suddenly of a cerebrovascular accident four months later.

The complication of pancreatic fistula might have been minimized by the use of a drain to the pancreatic area because the development of this fistula was preceded by a collection of fluid in

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the lesser sac and in the left upper quadrant, a condition which temporarily impaired his food intake. Otherwise his ability to eat and his general condition gradually and progressively improved up to the time of his sudden death.

CASE 2.—A. B., a 71-year-old white woman, was admitted on July 25, 1952, with a history of epigastric pain of six to eight months' duration, increasing in severity, with anorexia, a weight loss of 40 lb. (18.1 kg.), and tarry stools. She had mental changes thought to be characteristic of senile arteriosclerosis. Examination of the chest and cardiovascular system revealed no abnormalities.

Physical examination on admission to St. Luke's Hospital revealed no palpable nodes or masses; weight loss was pronounced and the skin pallid. The remainder of the physical examination was essentially noncontributory. The blood pressure was 160/80.

The red blood cell count was 1,700,000; hemoglobin, 5.8 gm. per 100 cc., and white blood cell count and differential distribution, normal. The patient was given supportive therapy of blood transfusions (3,500 cc.), vitamins, and a bland diet. After this, the red blood cell count was

Fig. 1 (Case 1).—Huge ulceration shown on lesser curvature. Its base was constituted by the pancreas.

5,200,000 and the hemoglobin content 14.2 gm. per 100 cc. Her general strength was fair, and she was able to walk without assistance. There was no dyspnea, and her color was good. X-ray examination of the chest revealed no abnormalities; the serum electrolytes, total protein, nonprotein nitrogen, and fasting blood sugar were all normal. The electrocardiogram was interpreted as showing "generalized myocardial damage." X-ray examination of the stomach revealed two large deep ulcer craters on the lesser curvature, the smaller ulcer at the angularis. The characteristics of the superior ulcer were such that it seemed to be fixed, but the mucosal pattern in the surrounding area seemed normal. The stomach wall near the ulcers was flexible to palpation during fluoroscopy.

At operation on Aug. 5, 1952, there was no gross evidence of malignant growth. Findings on general exploration of the abdomen were negative; the liver was normal. There was a fixed mass posteriorly in the region of the body of the pancreas with the stomach attached to it. A gastrotomy was done which revealed a large 7 by 3 cm. ulcer crater, with a dirty grayish base, lying on the posterior wall near the lesser curvature and fixed to the pancreas. There were slightly rolled edges, but they were sharp and discrete. The pancreas itself was movable. The smaller ulcer was 2 cm. in diameter and lay distal to the angularis just adjacent to the lesser curvature. There was no evidence of malignant growth and no enlarged nodes in the area. The stomach wall elsewhere was perfectly flexible. Biopsy from the edge of the ulcer crater revealed

only inflammatory tissue. By sharp dissection the stomach was removed from the pancreas, and a gastrectomy was performed with use of a posterior Polya-type gastroenterostomy. No drainage was employed. The patient tolerated the procedure very well, and she was discharged from the hospital eight days after operation. The barium meal prior to discharge showed a well-functioning gastroenterostomy. She was free of pain, her appetite was returning, and her general condition was good. When last seen, seven months after operation, her general condition was good.

CASE 3.—E. C., a 56-year-old man, was admitted to the Ellis Fischel State Cancer Hospital on March 20, 1946. For five years he had experienced intermittent epigastric distress with heartburn and abdominal cramps. On admission the blood pressure was 200/130; he had tenderness in the epigastrium, but no masses were palpable. Gastric analysis revealed blood and low acid content. The feces showed a 4+ guaiac reaction. The x-ray report was as follows: "The mucosa is effaced in the posterior lesser curvature aspect of the gastric corpus."

Fig. 2 (Case 2).—Roentgenogram showing two ulcers on lesser curvature. The smaller ulcer near the incisura was not attached to adjacent structures. Base of the upper was formed by the pancreas.

He underwent exploration on March 27, 1946. The stomach was found fixed in its midportion to the body of the pancreas. A gastrotomy was done, and a large ulcer with complete destruction of the gastric wall was found, the pancreas forming the base of the ulcer. There was no cancer in the biopsy specimens taken at the time of operation. The stomach was dissected free from the pancreas that formed the base of the ulcer. A subtotal gastrectomy was done with posterior gastroenterostomy, and the ulcer bed was allowed to remain *in situ*. A follow-up report on this patient disclosed that he committed suicide one year later and had been having abdominal pain prior to death. The ulcer measured 7.5 by 6.5 cm., and multiple sections of the lesion showed no carcinoma.

CASE 4.—C. T., a 40-year-old man, had a two-year history of epigastric pain relieved by food, with occasional vomiting. X-rays taken at the time of the initial admission to Ellis Fischel State Cancer Hospital in October, 1950, showed marked dilatation of the stomach with 90%

retention. The patient refused surgery and was given an ulcer diet. A small gastric ulcer had been noticed in the x-ray examination. During the ensuing months his symptoms became much worse, with pain and persistent vomiting.

He was readmitted in April, 1951, at which time no masses were palpable, although there was some upper abdominal muscle guard. The ulcer niche was found to be much larger on the x-ray studies at this time. An ulcer 8 cm. in diameter was seen on the posterior wall in the midcorpus. The crater was 5 cm. in depth, and the impression was that this represented a benign ulcer. At operation on April 20, 1951, the ulcer was found to be fixed to the body of the pancreas. Biopsies of nearby nodes were negative. The margins of the ulcer after gastrotomy were found to be piled up, a condition arousing suspicion of malignant growth, but multiple biopsy specimens were interpreted as benign. The ulcer crater involved the mesocolon as well as the pancreas. During the course of the gastrectomy, then "the ulcer was entered leaving the crater in place, dissecting the rest of the stomach free from the ulcer." The ulcer measured 9 by 7 cm. in diameter and in the pathological study was found to be entirely benign. The course was entirely satisfactory, and the patient was doing well in January, 1952.

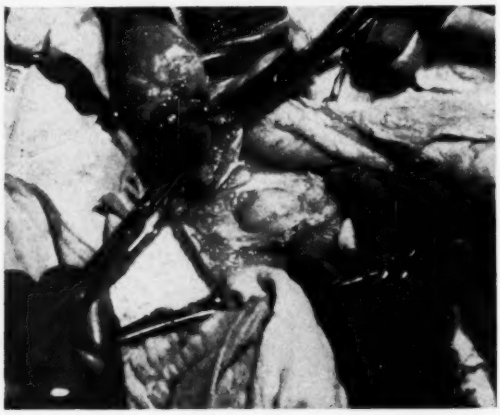

Fig. 3 (Case 5).—Ulceration of 6 cm. on posterior surface of stomach, showing penetration into pancreas with duodenum forming a large portion of the ulcer. Rim of the ulcer has been severed. Hole in the stomach is outlined by the tips of the hemostats.

Case 5.—C. A., a man, aged 70, was admitted to St. Luke's Hospital on Nov. 8, 1952, with a four-year history of intermittent epigastric cramping pain relieved by food. During this period he was treated medically, but he had grown progressively weaker prior to admission and had lost about 80 lb. (36.3 kg.), principally during the previous year.

About 13 days prior to admission, vomiting became a prominent feature, and he was admitted to a hospital where he was found to be vomiting blood rather persistently. During the week prior to admission a gastrointestinal series was done, which was interpreted as showing evidence of a carcinoma of the stomach with some degree of pyloric obstruction. He received blood before being transfered to St. Luke's Hospital.

The blood pressure was recorded as 100/70, pulse rate 72, and respirations 21. He was a cachectic elderly man, chronically ill. The outstanding features were frequent pvc's a harsh apical systolic murmur, slight tenderness in the epigastrium, and a small right inguinal hernia. On admission the laboratory data were as follows: red blood cell count 2,480,000, hemoglobin content 7.4 gm. per 100 cc., and normal differential distribution. Urinalysis showed nothing abnormal, and blood chemistry values were within normal limits. He was given whole blood shortly after admission. On the third day his abdomen became distended, with only a mild complaint of abdominal pain. Efforts to relieve the gas accumulation were unsuccessful, and an open plate of the abdomen showed pneumoperitoneum.

An exploratory laparotomy was done, and a perforation was discovered on the anterior surface of the stomach near the lesser curvature—pars media. A biopsy specimen was taken from the ulcer which showed only scar tissue. A considerable quantity of pus was evacuated from the abdomen, which was closed without drainage. The offending ulcer was rather large and could be felt to extend over the posterior surface of the stomach and onto the lesser curvature and anterior surface where it had perforated. It was felt that he was recovering satisfactorily until nine days after operation, when he suddenly began to experience hematemesis and multiple massive black stools. For the next five days control of hemorrhage was difficult. He had received 17 units of whole blood up until Nov. 24, 1952, at which time he appeared to be stable, and an attempt at surgical control of bleeding was decided upon.

A gastrectomy was performed with little difficulty. The stomach wall was freed from the ulcer base, which was constituted by the pancreas and the wall of the fourth portion of the duodenum. This ulcer measured 6 by 4 cm. in diameter, was very deep, and had destroyed the gastric wall over that area. An anterior Hofmeister anastomosis was performed.

His course required digitalization, chemotherapy, and parenteral administration of fluids. Abdominal distention became a problem and prevented early oral alimentation. His course was

Fig. 4 (Case 6).—Autopsy specimen. Large elongated ulcer involves lesser curvature, anterior surface, and greater curvature of the stomach near the pylorus. Perforation is seen directly toward the liver.

complicated by intestinal obstruction produced by adhesive bands, wound dehiscence, thrombophlebitis, and by a large pelvic abcess that had developed secondary to the earlier perforation. He died on Dec. 16, 1952.

No evidence of cancer was discovered at necropsy, thus confirming the operative diagnosis.

CASE 6.—R. H., a 77-year-old man, was admitted to St. Luke's Hospital on Jan. 9, 1953. He had had vague upper abdominal symptoms for 10 to 15 years, without medical attention. His symptoms increased in severity during two months prior to admission, with anorexia, a weight loss of about 60 lb. (27.2 kg.) tarry stools, nausea, and vomiting.

In the hospital no masses were palpable, and, except for his cachectic state and complaint of severe upper abdominal pain, no physical findings were notable.

The gastrointestinal series revealed duodenal deformity without obstruction. Gastric analysis showed total acidity 20 degrees, free acidity 0 degrees. A guaiac test of the stool was positive. Extensive blood chemistry tests were all within normal limits. The red blood cell count was 4,010,000; hemoglobin, 13.1 gm. per 100 cc., and white blood cell count, 9,600.

The patient's course in the hospital continued in character similar to that prior to admission, with constant pain but with few physical findings. There were no findings to indicate that a catastrophe had taken place. He died suddenly, 11 days after admission.

Postmortem findings proved the cause of death to be a huge gastric ulcer 6 cm. in length and 2 cm. in width located near the pylorus and situated directly perpendicular to its long axis. It extended from the anterior surface around the lesser curvature, with no attachment to nearby structures. On the anterior surface there was a large perforation. The walls of the ulcer collapsed easily against each other, thus accounting for the few findings on the x-ray series.

CASE 7.—W. B., a 73-year-old white man, was admitted to St. Luke's Hospital on Feb. 13, 1953, and he died one and one-half hours after admission. There was a one-year history of anorexia and a 20 lb. (9.1 kg.) weight loss but no abdominal pain or symptoms or bleeding. About four or five days prior to admission he began having four or five tarry stools daily, with fainting and vomiting of gross blood. He was first seen on the day of admission in a state of collapse. Aside from shock and gross gastrointestinal bleeding, the physical examination showed nothing significant. No masses or enlarged nodes were found. He failed to respond to the rapid infusion of 5 units of whole blood and died.

Fig. 5 (Case 7).—Fixed autopsy specimen. Pancreas forms the base of this ulcer which measured 9 cm. in the fresh state. Splenic artery is represented by the projection near the margin closest to the ruler. Esophagus is seen in upper right portion of photograph.

The postmortem examination revealed a huge ulcer of the posterior wall of the stomach situated in the upper pars media. It had penetrated into the pancreas, and the splenic artery could be seen to enter the ulcer base. The pancreas itself was not attached posteriorly. No grossly enlarged nodes were found, and no evidence of abdominal tumor was to be seen. The ulcer measured 9 cm. in the fresh state. The edges were smooth, the mucosa was not piled up, and the base was a grayish-yellow slightly nodular surface. Multiple radial sections through the ulcer showed no evidence of cancer; only the cicatrix and cellular infiltration of a chronic benign ulcer of the stomach penetrating into the pancreas and splenic artery.

COMMENT

In the older literature there is little written on the subject of these enormous ulcers save to note that they occasionally were found at autopsy and proved to be benign. Case reports have appeared sporadically in more recent years which collectively indicate that such ulcers frequently terminate in death for the patient by massive hemorrhage or through cachexia with its concomitant secondary factors. The clinical course is usually a prolonged one with variable abdominal symptoms in no way distinguishable from those of the smaller gastric ulcers or from malignant lesions of the stomach.

Incidence.—Some statistical estimates have been published and are presented in outline form in Table 1. Of more importance than the relative infrequency of these huge ulcers is the fact that they are more likely to be benign than has been generally thought. In 1928 Alvarez and MacCarty presented a statistical analysis from which inferences were drawn concerning the relationship between the size of the ulcer and its nature. These authors concluded that "differences of opinion will seldom arise in the diagnosis of lesions more than four centimeters in diameter because most of them are definite tumors, the nature of which is fairly obvious to clinicians, roentgenologists, surgeons and pathologists." Of their 638 cases of gastric ulcer in which the patients were subjected to surgery, 9 were found in which a benign ulcer measured more than 1,000 sq. mm., and none of these ulcers were over 4 cm. in diameter. Of these nine, it was demonstrated that five had possibly been malignant, as shown in the subsequent clinical course, or else there was some doubt as to the correctness of the original diagnosis. By inference this study indicated that ulcers of large size are almost certainly malignant. These inferences have been repeated as recently as 1950.[1]

TABLE 1.—*Incidence of Neoplasms Among Gastric Ulcers of Large Size*

Author	Cases, No.	Neoplasms	Benign	Verification
Ledoux-Lebard *	13 (above 4 cm. diam.)	4	9	Histologic study
Brule and Hillemand †	11 (above 4 cm. diam.)	4	7	Histologic study
Matthiew and Moutier	3 (above 12 cm. diam.)	0	3	Histologic study
Our series	7 (above 6 cm. diam.)	0	7	Histologic study

* Of 28 cases reported, 24 were benign; however, not all were proved by histologic study.
† Four additional cases were benign by clinical study.

It seems clear from these estimates in Table 1 and from our own experience that the giant ulcer—and we carefully emphasize that they are very large—is at least as likely to be benign as malignant. Recognition of this fact is particularly important, for if such an ulcer is erroneously diagnosed as malignant, the patient may be subjected to total gastrectomy and/or needless resection of adjacent organs such as the pancreas or portions of the liver.

Some of the huge penetrating lesions have been found to be associated with a mass of inflammatory tissue which may in some instances be palpable. It is this finding which Ledoux-Lebard [2] has referred to as "pseudotumorous" and which may serve to confuse the diagnosis to an even greater extent.

Clinical Characteristics.—The characteristics most prominent in some of these cases are the long duration of symptoms and massive hemorrhage. It should be noted that the clinical findings may be minimal. Ulcers of this magnitude have been discovered in very young persons and in those with mild gastrointestinal symptoms of very brief duration.

Gross Characteristics.—The ulcers considered herein are penetrating to such an extent that the entire thickness of the gastric wall over a large area is destroyed. They involve the anterior or posterior surface and often both, extending over the

1. Comfort, M. W.: Cancer **3**:520, 1950.
2. Ledoux-Lebard, Y.: Arch. mal. app. digest. **34**:207, 1945.

lesser curvature as well. The defect in the gastric wall is, in effect, plugged by some adjacent organ, such as the pancreas or liver (those most frequently involved), or the anterior abdominal wall, transverse mesocolon, or tissues at the splenic hilus. The stomach thus becomes fixed, and the adjacent organ actually constitutes the ulcer base. In two instances (Cases 5 and 6) perforation into the free peritoneal cavity occurred after the patient had been admitted to the hospital for treatment. In Case 5 severe hematemesis and melena were the presenting symptoms and in Case 6 abdominal pain. However, perforation seems to be a rare occurrence among other reports of ulcers of this category.

From the large amount of scar that develops in the area of ulceration and the degree of fixation of the stomach, it at once appears that such findings might easily be mistaken for cancer. In those specimens examined thoroughly at postmortem and at operation there has been no histological evidence of carcinoma. It is true that occasionally a large lymphosarcoma of the stomach may be confused with this type of benign ulcer; however, that diagnosis can usually be made by utilizing the frozen-section biopsy.

TABLE 2.—*Clinical Course of Giant Gastric Ulcers*

Case	1	2	3	4	5	6	7
Age, yr.	55	71	56	40	70	77	73
Duration of symptoms	7 mo.	8 mo.	5 yr.	2 yr.	4 yr.	10 yr.	1 yr.
Character of symptoms	Pain, anorexia	Pain, anorexia	Pain	Pain, emesis	Pain	Pain	Anorexia, G.T. bleeding
Massive hemorrhage	No	Yes	No	No	Yes	No	Yes

TABLE 3.—*Clinical Course of Giant Gastric Ulcers*

Case	1	2	3	4	5	6	7
Weight loss	Yes (25 lb.)	Yes (40 lb.)	No	No	Yes (80 lb.)	Yes (60 lb.)	Yes (20 lb.)
Perforation into free peritoneal cavity	No	No	No	No	Yes	Yes	No
Obstructive syptoms	No	No	No	No	No	No	No

Diagnostic Methods.—The roentgenologic study of the gastrointestinal tract is generally the first and most informative diagnostic adjunct. The following features may be helpful in the evaluation of a large gastric defect: The presence of very deep ulceration with little derangement of the surrounding mucosal pattern, the radiating pattern of mucosal folds, and the pliability of the surrounding gastric wall serve to indicate that the lesion is benign. It is well known that a posterior ulcer, even a very large one, may be overlooked in the roentgenologic study unless particular care is taken to demonstrate the lesion, and even then some very large ulcers may not be found roentgenologically. Recent studies of this problem indicate that the large defect may so distort the stomach that many of the features of cancer may be found in the roentgenologic study.[3]

Gastroscopy is an excellent means of locating the ulcer accurately and visualizing its gross characteristics. The gastroscopist, like the radiologist, however, should not make a diagnosis of cancer because of the size of the lesion alone.

3. Elliott, G. V.: Personal communication to the authors.

It is our contention that an accurate decision as to the nature of the process in an ulcer that has assumed enormous size can and should be made at the operating table on the basis of the gross examination and the microscopic study of frozen tissue. This can be accomplished by (1) biopsy of regional lymph nodes or (2) gastrotomy with multiple biopsies of the ulcer edge. There are no valid objections to such biopsies, and they give a quick answer to the important question of whether one is operating for a cancer or for a benign ulcer.

Surgical Treatment.—A second reason for holding that the huge benign penetrating ulcer of the stomach demands surgical intervention is the need for correction of a gross physical defect in the stomach wall because of its serious potentialities. The pronounced failure of the ulcer to heal and the hazard of possible massive

TABLE 4.—*Diagnosis of Giant Gastric Ulcers*

Case	1	2	3	4	5	6	7
X-ray interpretation	Huge gastric defect ? lymphosarcoma	Two gastric ulcers, one huge benign	Large posterior ulcer ? malignant	Huge ulcer ? benign	Huge ulcer malignant	Duodenal deformity	None
Gastroscopy interpretation	Large ulcer lesser curvature interpretation malignant	.....	.....	.....	.....	.....	.....
Biopsy	Gastrotomy frozen section	Regional node and gastrotomy frozen section	Gastrotomy and frozen section	Regional node and gastrotomy, frozen section	Biopsy of ulcer edge	Autopsy	Autopsy
Ulcer size	7 cm. diam.	7 x 3 cm.	7.5 x 6.5 cm.	9 x 7 cm.	6 x 4 cm.	6 x 2 cm.	9 cm. diam.

TABLE 5.—*Treatment of Giant Gastric Ulcers*

Case	1	2	3	4	5	6	7
Surgery	Separation of stomach from pancreas; closure of gastric defect	Separation leaving ulcer base intact; gastrectomy	Same as Case 2	Separation leaving ulcer base intact; gastrectomy	1st operation closure of perforation; 2d operation, same as Case 4	None	None
Result	Good operative result; died of cerebrovascular accident 4 mo. postop.	Good 8 mo. postop.	Continued pain; suicide at 1 yr.	Good 2 yr. postop.	Death from (*a*) pelvic abscess, (*b*) intestinal obstruction, (*c*) thrombophlebitis, (*d*) pneumonia	Death from perforation	Death from massive hemorrhage

hemorrhage, free perforation, continued weight loss, and persisting symptoms constitute a dire threat to life.

There has been some difference of opinion as to the proper surgical approach. Some authors in the past have favored an initial procedure designed to allow alimentation and improvement both in the general condition of the patient and in the tissues locally involved in the ulcerative process. We feel that in cases in which there is extreme malnutrition without hemorrhage, a preliminary jejunostomy may be of great value. In general, it is incumbent upon the surgeon to employ the method which is best suited to the needs of the patient.

In our cases a direct attack upon the ulcer has been preferred after the diagnosis is established. A simple and adequate procedure for handling these large lesions can be designed to release the stomach wall from the adjacent structure to which it has become attached. A large hole in the stomach wall is thereby created without

disturbing the organ which forms the ulcer base. When, for example, the stomach is densely adherent to the pancreas, sharp dissection of the scarred rim of the ulcer may obtain release of the stomach without the risk involved in excising the base of the ulcer from out of the pancreas or in resecting the pancreas. The gastrectomy is thus greatly facilitated and a difficult and complex situation converted into a relatively simple one. In the first case presented, because of the patient's poor condition it was considered unwise to proceed with gastrectomy, and a simple closure of the large gastric defect was done after freeing it from the ulcer bed in the pancreas. In this instance no drainage was instituted from the region of the pancreas, and a spontaneous pancreatic fistula developed through the operative incision. This closed spontaneously, and the end-result was entirely satisfactory. In the remainder of cases reported no drainage was employed. No complications appeared which would be attributed to failure to drain. No apparent ill effects followed leaving the well-scarred base of the ulcer in its place without any attempt to excise, close, or cover it, whether in the pancreas, liver, or abdominal wall. However, the decision as to drainage must be determined according to the individual situation at hand. It is apparent that the problem presented in Cases 1 to 5 would not have confronted the surgeon in Case 6 because, although the ulcer was large, there was no attachment to any extragastric structure.

SUMMARY

A survey of the incidence, characteristics, and treatment of giant-sized benign penetrating gastric ulcers is presented.

The importance of establishing a correct differentiation from cancer in these huge ulcers prior to definitive treatment is emphasized. This can be accomplished by recognizing certain roentgenologic and gross characteristics combined with histologic study.

Surgical intervention is strongly advocated because of the uncertainty of the clinical diagnosis, the pronounced failure of the defects to heal, and the danger of massive hemorrhage.

Attention is directed to a surgical method of managing such lesions by the conversion of a situation which might demand total gastrectomy or resection of adjacent organs into one of partial gastric resection or closure of the defect in the gastric wall after dissection of the stomach from the ulcer margin.

Seven cases illustrating the management of patients with such ulcers are presented.

DISCUSSION

Dr. C. M. Schroeder, Milwaukee: Drs. Shoulders and Lischer have brought to our attention a problem that bothers all of us who deal with gastric lesions.

[Slide] The data on this slide indicate criteria which have been used as points of differentiation between ulcer and cancer and reveal some of the sources of confusion. This study is based on 91 patients who were operated on at the Veterans Administration Hospital in Milwaukee, with preoperative diagnoses of benign ulcer. Eleven cancers (12%) were found at operation.

It is interesting to note that the roentgenologists suspected malignant growth in 25% of the benign lesions and in 30% of the cancers. Gastroscopy indicated cancer in 25% of the benign lesions and in one-sixth of the cancers.

The duration of symptoms in the cancer cases averaged 4½ years, from 2 months to 12 years.

Two cases illustrate the importance of making an accurate diagnosis—as emphasized by the authors—before embarking upon a definite procedure.

[Slide] This reproduction of a stomach x-ray of a 61-year-old man was interpreted as showing an obstructing lesion of the distal third of the stomach. At operation a large mass was found high in the lesser curvature, which had not been apparent from the x-ray. Because of its size, it was thought to be cancer, and total gastrectomy was done. Histologic study proved it to be a benign ulcer. Although the patient has been fortunate (he gained weight and is now eating three meals a day, five years after operation), an unecessarily radical and hazardous operation was performed. As a matter of fact, his only complaint now is his reduced capacity for beer, and in Milwaukee that is quite a handicap.

In another case the operator's inability to make a correct diagnosis from the gross appearance resulted in death from cancer in the gastric remnant in which a supposedly benign ulcer had been left behind at the time of gastrectomy, apparently from the operator's impression of the difficulty of excising it.

In three cases, benign ulcers have occurred on the greater curvature (however, in each instance there were multiple ulcers present).

Because of the difficulty of diagnosis of benign lesions, because of the not too successful medical management of gastric ulcer, and because of the low mortality for resection for gastric ulcer (1.25% in our series), our surgical staff recommends resection for all gastric ulcers. Every ulcer is regarded as potentially malignant.

Preoperative preparation for all gastric lesions includes preparation of the bowel so that a substitute stomach can be constructed of an intestinal segement if a total gastrectomy is done. The patient is placed on the table so that a combined thoracoabdominal approach can be used if desired. When the nature of the lesion has been determined (by frozen section, if necessary), the appropriate resection is done.

EVALUATION OF PROTEIN AND FAT METABOLISM IN POSTGASTRECTOMY PATIENTS

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IN A FOLLOW-UP study of 699 patients who had undergone gastrectomy Rauch reported [1] that slightly over 80% lost weight after surgery (an average weight loss of 13.8 lb., or 6.3 kg., in a patient with peptic ulceration). Others [2] have reported a somewhat lower incidence. While many such patients undoubtedly had minimal weight losses and others may have been on voluntary reduction diets, the frequency and magnitude of this complication led us to investigate further the possible causes. Faulty digestion and absorption of foodstuffs has been suggested [3] as a cause for

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the failure of postgastrectomy patients to gain weight. It has been intimated [4] that the degree of interference with the digestion of oral nutrients might be dependent on the type of anastomosis performed. In general, there are three types of anastomoses employed to reestablish the continuity of the gastrointestinal tract after a subtotal gastric resection: the gastroduodenostomy, the gastrojejunostomy with the efferent loop attached to the greater curvature, and the gastrojejunostomy with efferent loop attached to the lesser curvature. The last two can be varied by placing the jejunal loop retro- or antecolic. Some observers [5] assert that a gastroduodenostomy will better ensure digestion and absorption of carbohydrate, fat, and protein, because it restores the continuity of the gastrointestinal tract to nearer normal than the other types of anastomoses.

The present study was attempted in order to evaluate critically digestion in postgastrectomy patients, some who had maintained their weight, as well as others who had lost weight, being studied. It soon became apparent that factors other than digestion played a major role. The most significant problem encountered was the presence and severity of the "dumping syndrome." Thus, additional studies were done to determine the significance of the other factors involved in the loss of weight.

PROCEDURE AND METHODS

The eight patients studied were at least six months after resection, and none had had any recurrence of an ulcer either symptomatically or roentgenographically. Four of the patients had lost or failed to gain weight. Three of these had a fairly pronounced "dumping syndrome," which prior to admission might well have led to an inadequate caloric intake. The fourth patient (J. R.), who was undernourished, had peculiar lifelong restricted dietary habits.

Eight patients exhibiting the various types of anastomoses (gastroduodenostomy, isoperistalic gastrojejunostomy, and antiperistaltic gastrojejunostomy) were admitted to the Metabolic Unit of University Hospitals of Cleveland for a period of 12 days. Prior to admission each patient was interviewed by the dietician and the physician in charge of the metabolic unit so that an adequate well-rounded diet could be planned for the patient in advance. Strong iodine solution U. S. P. (Lugol's solution) (10 minims [0.6 cc.], three times a day) was given for the three days prior to the onset of the study to prevent the uptake of I^{131} by the thyroid.

All foods and fluids ingested were accurately measured and analyzed. Urine and feces were collected daily, and patients were instructed that any mixing of urine and feces invalidated the study. These excreta were then measured and analyzed. At the start of the study each patient was given a distilled-water enema, and this was discarded. Subsequently, distilled-water enemas ended each period, and these were included with the stool collected during that period. Patients all voided at 6:30 a. m., and this constituted the end of the 24-hour period.

The following four tests were done on each patient:

Oral I^{131} Protein Test.—On the morning following admission, in accordance with the method previously reported,[6] the patient was given a calculated amount of an iodinated protein-gelatin mixture. For three days following the administration, the urine was collected in 24-hour

4. (*a*) Lázár, D.: Über die Operationsverfahren des Magen- und Duodenalgeschwürs an Hand von Spatuntersuchungen bei 100 Magenresezierten, Zentralbl. Chir. **77**:1488-1497, 1952. (*b*) Clagett, O. T., and Waugh, J. M.: Indications for and Advantages of Schoemaker-Billroth I Gastric Resection, Arch. Surg. **56**:758-765, 1948. (*c*) Bohmansson, G.: Prophylaxis and Therapy in Late Postgastrectomy Complications, Acta med. scandinav., Supp. 246, pp. 37-45, 1950.

5. (*a*) Machella, T. E.: Symposium on Some Aspects of Peptic Ulcer: Mechanisms of the Post-Gastrectomy Dumping Syndrome, Gastroenterology **14**:237-255, 1950. (*b*) Footnote 4*b* and *c*.

6. Chinn, A. B.; Lavik, P. S.; Stitt, R. M., and Buckaloo, G. W.: Use of I^{131}-Labeled Protein in the Diagnosis of Pancreatic Insufficiency, New England J. Med. **247**:877-880, 1952.

periods, and the I^{131} content of each specimen was determined. The pooled 72-hour stool specimens were also quantitated for I^{131}. The amount of I^{131} found in the urine and in the stool was expressed as per cent of the administered dose.

Metabolic Dietary Studies.—During the time the I^{131} studies were being carried out, the patient was placed on a constant diet in which the nitrogen, carbohydrate, and fat content were known. This diet contained 70 or 80 gm. of fat per day, 1 gm. of protein, and 30 Cal. per kilogram of body weight. For the next six to eight days, the 24-hour urine specimens and the pooled stool specimens (for two to four days) were separately analyzed in duplicate for nitrogen by the macro-Kjeldahl technique. The percentage of fat in two fecal specimens from each patient was determined, following a modification of the method of Fowweather.[7] Since the study was being directed toward determining whether abnormally large amounts of nitrogen or fat were lost in the stool, rather than establishing whether the patient was in positive or negative nitrogen balance, a more prolonged period of study was not felt necessary.

Oral Glucose Tolerance Test.—Patients were given 1 gm. of glucose per kilogram of body weight, and hourly blood samples were taken for four hours after ingestion of the glucose. Blood sugars were determined by the Folin-Wu method. Blood specimens were drawn every 5 to 10 minutes for the first hour from two patients who exhibited a severe "dumping syndrome" in order to determine any abnormalities in the early portion of the curve. This was done to see if there was a correlation between the blood sugar levels and the onset of symptoms.

Roentgenological Studies of Upper Gastrointestinal Tract.—Each patient was examined fluoroscopically by an experienced roentgenologist in the presence of one of the investigators, and the functional and anatomical findings were evaluated after examination of the roentgenograms.

RESULTS

All patients in the symptomatic and asymptomatic groups had normal values for fecal excretion of nitrogen as determined both by using I^{131}-labeled protein and by direct measurement (Charts 1 and 2). The I^{131} excretion was not recorded for one of the patients, owing to the contamination of the stool specimen with urine.

All patients had fecal fat values which fell within normal limits,[8] although one subject, R. P., had a borderline value (Table). Since this patient had a moderate gain in weight and because his other studies were normal, it was believed that no digestive defect was present.

Three of our four symptomatic patients had the steep glucose tolerance curves (Chart 3) indicative of rapid carbohydrate absorption previously noted by other observers,[9] although the blood levels were not as high as have been reported.[9a,b] Two to three hours after ingestion of the glucose the blood sugar level of all patients fell significantly below their fasting control values.[10] In no patient was there any association between the onset of symptoms and abnormal blood glucose concentrations.

In many other cases, as well as the ones presented, the roentgenological study of the upper gastointestinal tract revealed a constant difference between the symptomatic and the asymptomatic groups. All patients exhibited a rapid emptying of the stomach, regardless of the type of anastomosis. Those who complained of the

7. Hawk, P. B.; Oser, B. L., and Summerson, W. H.: Practical Physiological Chemistry, Ed. 12, Philadelphia, The Blakiston Company, 1947, p. 409.

8. Footnote 3*a*. Footnote 7.

9. (*a*) Zollinger, R. M., and Hoerr, S. O.: Gastric Operations: Troublesome Postoperative Symptoms with Special Reference to Carbohydrate Ingestion, J. A. M. A. **134**:575-579, 1947. (*b*) Glaessner, C. I.: Disturbances in Sugar Metabolism After Subtotal Gastrectomy, Am. J. Digest. Dis. **12**:157-162, 1945. (*c*) Machella.[5a]

10. (*a*) Gilbert, J. A. L., and Dunlop, D. M.: Hypoglycaemia Following Partial Gastrectomy, Brit. M. J. **2**:330-332, 1947. (*b*) Zollinger and Hoerr.[9a]

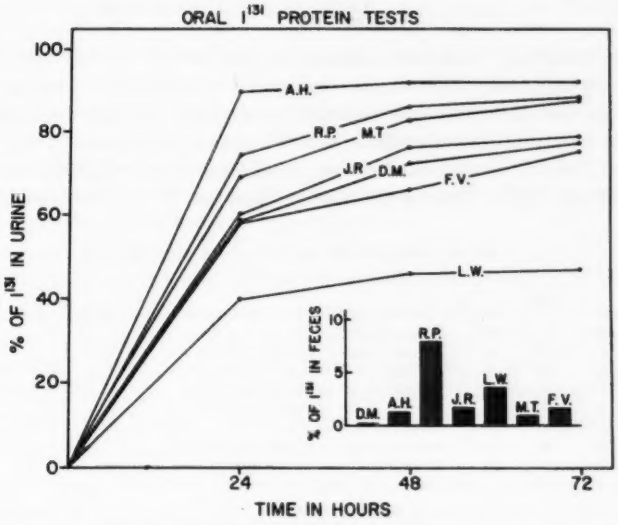

Chart 1.—Oral I^{131} protein tests. Normal individuals excreted 8% or less of the ingested isotope in the stool and between 50 and 90% in the urine. The amount of I^{131} in the stool of patient R. P. was at the upper limit of normal. On the other hand, L. W. had slightly less than normal amounts in the urine. Because all other tests in these two patients were within normal limits, it was thought that the two results mentioned above were not of sufficient magnitude to denote abnormal digestion and absorption of protein.

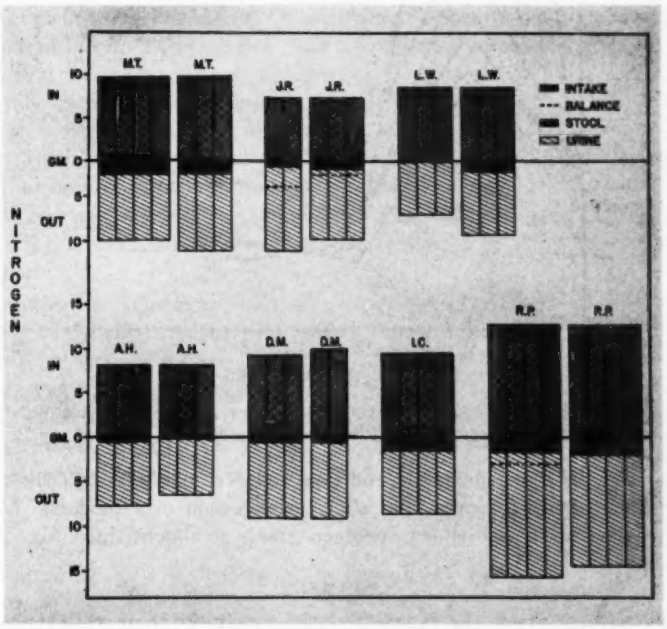

Chart 2.—Nitrogen balance studies. While a negative nitrogen balance occurred in a few instances, the amount of nitrogen lost in the stool was within a normal range.

"dumping syndrome," however, showed incomplete or delayed emptying of the duodenum or jejunum, which was not seen in the symptom-free patients. After 100 to 200 ml. of barium was ingested, it would pass rapidly through the anastomosis but would then be partially or completely delayed, causing a segment of the upper small intestine to distend. The peristaltic waves would increase, and gradually the affected segment would empty. During the time of distention the patient would have symp-

Type of Anastomosis and Per Cent of Fecal Fat

Patient	Age, Yr.	Sex	Type of Anastomosis Following Subtotal Gastrectomy	% of Fecal Fat
A. H.	39	F	Gastroduodenostomy	11.3
R. P.	50	M	Efferent loop to greater curvature	22.8
D. M.	52	F	Efferent loop to lesser curvature	16.4
I. C.	47	F	Efferent loop to lesser curvature	11.8
L. W.	58	F	Efferent loop to lesser curvature	19.3
J. R.	66	M	Gastroduodenostomy	13.2
M. T.	46	F	Efferent loop to greater curvature	12.5
F. V.	58	M	Efferent loop to greater curvature	....

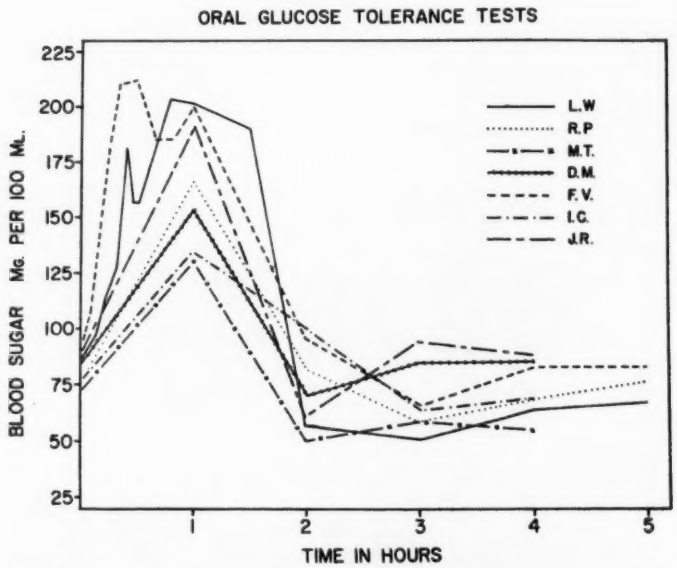

Chart 3.—Oral glucose tolerance tests. While hyper- and hypoglycemia occurred, these changes took place after the symptoms of the "dumping syndrome."

toms consistent with the "dumping syndrome." Interestingly enough, these findings were observed fluoroscopically only after the ingestion of a moderate amount of barium, whereas in the subsequent roentgenograms no abnormalities were apparent.

COMMENT

In the present study the failure to gain weight in these patients cannot be ascribed to any abnormality in the digestion and absorption of protein or fat on the basis of the results with I^{131}-labeled protein, stool nitrogen, or fecal fat content.

Only one patient, R. P., had fecal fat values which were at the upper limit of normal. This patient has gained weight and has been symptom-free since operation. These patients further showed little or no abnormality in their ability to digest protein and fat or to absorb glucose, regardless of the type of anastomosis employed. Inadequate digestion and absorption of fat has, however, been reported following vagotomy [11] and total gastric resection.[3e] It has also been noted after radical subtotal gastrectomy, especially when combined with vagotomy.

Some observers [12] have attempted to ascribe the symptoms characteristic of the "dumping syndrome" to either hyper- or hypoglycemia, but, similar to our results, they report the onset in many patients shortly after ingestion of the glucose and not later, when the high or low blood sugar levels were encountered. Many patients' blood glucose concentration reached hypoglycemic levels two to three hours following the ingestion of carbohydrate, and yet they were asymptomatic at that time. In a few cases, true mild hypoglycemic symptoms appeared, but they differed from those characteristic of the "dumping syndrome."

In one patient, L. W., who exhibited marked "dumping" symptoms, the insertion and inflation of a balloon in the efferent loop reproduced her symptoms, which were relieved by deflating the balloon.[5a] Injection of barium through the tube or swallowing of it reinstituted symptoms, which subsided when the barium was drawn off.

Another patient, F. V., had a severe "dumping syndrome," which was most marked in the morning. On his being given the glucose test meal he had the typical flushing, sweating, palpitation, and weakness, similar to the reaction that frequently occurred after he ate his breakfast. A blood sugar drawn at this time was 104 mg. per 100 ml. of blood. Three ounces (30 cc.) of a concentrated fat emulsion [13] was given the next morning, and again the symptoms were reproduced but were relieved subsequently after an emesis containing most of the ingested fat and a large amount of bile. However, when the fat mixture was given in small divided doses (30 ml. five times a day), it was well tolerated. A month after discharge he gained 8 lb. (3.6 kg.), apparently because of the added caloric intake from the ingestion of these small supplementary feedings. Each of these patients had at least 80% or more of the stomach resected. In one the anastomosis was isoperistaltic, and in the other, antiperistaltic.

In summary, a segment of the gastrointestinal tract becomes distended in the presence of a relative anatomical or functional obstruction dependent on the volume of ingested and secreted material, which results in a feeling of fullness, nausea, and discomfort and occasionally palpitations and flushing. This in turn may result in anorexia, which may explain the weight loss without abnormalities in digestion. Aerophagia, which occurs in the presence of a partial obstruction or delayed emptying, may intensify the belching and pyrosis commonly found in these patients.

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11. Fox, H. J., and Grimson, K. S.: Defective Fat Absorption Following Vagotomy, J. Lab. & Clin. Med. **35**:362-365, 1950.

12. Schechter, S. E., and Necheles, H.: Postprandial Symptoms Following Subtotal Gastrectomy for Peptic Ulcer and Their Relationship to the Glucose Tolerance Curve, Gastroenterology **12**:258-274, 1949. Zollinger and Hoerr.[9a] Glaessner.[9b] Gilbert.[10a]

13. The oral fat emulsion (Ediol) employed was supplied by the courtesy of Charles E. Dutchess, M.D., Medical Director of the Schenley Laboratories, Inc., New York.

Many observers [14] are in agreement with our impression that distention of the anastomotic loop produced by the rapid emptying of the stomach, which occurs in reverse proportion to the amount resected, is the most likely cause of the "dumping syndrome."

CONCLUSIONS

1. Little, if any, disturbance in the ability to digest and absorb protein and fat or to absorb glucose was found in four undernourished postgastrectomy patients.

2. The most apparent cause of weight loss or the inability to gain was an inadequate caloric intake due to the "dumping syndrome" or the fear of producing symptoms.

It is our impression from the cases presented and from others more recently studied that these late complications of subtotal gastrectomy are more frequent the higher the resection and that they bear little or no relation to the type of the anastomosis employed.

Technical assistance was given by G. Warren Buckaloo, M.S., of the Department of Radiology.

DISCUSSION

DR. ROBERT M. ZOLLINGER, Columbus, Ohio: I rise to congratulate the authors. I think this is a very valuable contribution.

Of course, in Ohio we stick together, as you probably know, but I think there has been so much emphasis on the incidence of recurrent ulceration, decreasing mortality, and so forth, that we tend to forget what happens to some people after they have various types of gastric procedures. I think some 10 or 12% of these persons, even in the most optimistic reports, do have some difficulties. Certainly, in the animal, the more stomach you take out, the greater difficulty the animal has in recovering his original weight, and in our studies we found the same thing to be true.

In our series of fat balance studies, unlike those reported by Dr. Babb, we think there is some relationship between the fat absorption and the amount of stomach resected. Furthermore, there is a decrease following vagus section. This same decrease shows up after the Billroth-I type of anastomosis, which is a little bit disappointing to some of us.

However, I don't believe this decrease in fat absorption, as they say, has much to do with the patient's nutrition. Perhaps those individuals who have had better results with gastric resection have had it because they had at least a third of their stomach remaining.

In selecting the type of operation for duodenal ulcer, I wonder whether or not we should pay more attention to the patient's preoperative nutritional status. By that I mean that we tend—in these persons weighing 130 or 140 lb. (59.0 or 63.5 kg.)—to leave in more stomach than in the rather obese patient. At present we prepare to resect about a third of the stomach, section the vagus nerve, and do a full-width gastroduodenosomy of the Billroth-I type. The Scandinavians have reported on some postgastrectomy patients with nutritional difficulty who have been restored to normal health by converting the Billroth-II type procedure to Billroth-I. I think we should keep the factor of nutrition in mind when planning our gastric procedures.

These nutritional studies should be continued, because, although the over-all result per hundred may look pretty good, many patients are nutritional problems following extensive gastric resection.

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14. Hinton, J. W.: The Evaluation of End Results in Physiologic Versus Pathologic Operative Procedures for Chronic Duodenal Ulcer During the Past 2 Decades, Ann. Surg. **132**:641-651, 1950. Farmer, D. A.; Howe, C. W.; Porell, W. J., and Smithwick, R. H.: The Effect of Various Surgical Procedures upon the Acidity of the Gastric Contents of Ulcer Patients, ibid. **134**:319-331, 1951. Walton, J.: Progress of Gastric Surgery in the Last Half-Century, Brit. M. J. **1**:206-210, 1950. Johnson, H. D., and Orr, I. M.: A Surgical Policy for Peptic Ulcer, Lancet **1**:253-257, 1953. Muir, A.: Postgastrectomy Syndromes, Brit. J. Surg. **37**:165-178, 1949.

GASTRIC SECRETION IN THE IMMEDIATE POSTOPERATIVE PERIOD

JAMES C. DRYE, M.D.
ARTHUR M. SCHOEN, M.D.
AND
GEORGE SCHUSTER III, M.D.
LOUISVILLE

THIS STUDY was stimulated by the development of severe hemorrhage from peptic ulcers in four patients during convalescence from operations not related to the stomach or duodenum, and by a severe hemorrhage from a posterior duodenal ulcer in a patient nine days after suture of an anterior duodenal perforation. All the ulcers either were known to exist prior to surgery or were found to be old ulcers from their gross or histological appearance. However, with the exception of the case of hemorrhage following suture of an anterior ulcer, none showed clinical evidence of activity in the preoperative period. All were true peptic ulcers and not related to the Curling ulcer or to the erosions commonly found in the gastrointestinal tract at autopsy.

REPORT OF CASES

CASE 1 (No. 9693, St. Anthony's Hospital).—G. R., a 63-year-old white man, admitted on Dec. 6, 1950, bled on the 14th postoperative day following the nailing of a traumatic hip fracture. There was no history of peptic ulcer. At autopsy a chronic callous benign ulcer was found on the lesser curvature of the stomach. In the bed of the ulcer there was a large open vessel.

CASE 2 (No. 7144, St. Anthony's Hospital).—O. M., a 46-year-old white man, was admitted, Aug. 2, 1952, for an open comminuted fracture of the humerus. There were questionable signs of a ruptured abdominal viscus which subsided within 12 hours. The patient had a 15-year history of ulcer and had had perforation 10 years before. His illness ran an uneventful course for 21 days. Then, he suddenly went into shock from hemorrhage and died within two hours. Autopsy showed a fibrinous exudate over the peritoneum. There was a posterior duodenal ulcer which had penetrated the gastroduodenal artery.

CASE 3 (No. 105523, Norton Memorial Infirmary).—W. M., a 47-year-old white man, was admitted, Aug. 25, 1951, with a cancer of the rectosigmoid. He was known to be hypertensive. He had had ulcer symptoms for 15 years, and x-ray studies four years before had shown a duodenal ulcer. There had been no recent clinical evidence of activity. The carcinoma of the rectosigmoid was removed by a combined abdominoperineal resection. After seven days of an uneventful recovery, he suddenly bled. After 12 hours of observation, a gastric resection was done because of uncontrollable bleeding. A posterior duodenal ulcer was found, and it had penetrated the gastroduodenal artery. He died on the second postoperative day.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 7, 1953.

This work was supported in part by a grant from the National Institutes of Health, United States Public Health Service.

From the Department of Surgery (Drs. Drye and Schuster) and the Department of Medicine (Dr. Schoen), University of Louisville School of Medicine.

CASE 4 (No. 25579, Louisville General Hospital).—T. K., a 63-year-old derelict, was admitted, Sept. 5, 1952, because of bloody diarrhea of two days' duration. A previous admission had disclosed moderately advanced pulmonary tuberculosis, epilepsy, syphilis, hypertensive heart disease, and chronic alcoholism. During the first five days after admission, he continued to pass red blood by rectum, and 16 pints (8 liters) of blood was required to keep his count within reasonable limits. At no time did he vomit blood, and repeated aspirations of the stomach never disclosed any blood. Because of continued bleeding, the abdomen was explored. The colon was found to be full of blood. There was no blood in the small intestine. There were many diverticula in the sigmoid colon, but no other abnormality was found. A resection of the sigmoid was done with an end-to-end anastomosis. The next morning the patient vomited blood for the first time. Because of uncontrollable hemorrhage, the abdomen was reexplored and a gastric resection was done. The stomach and jejunum were filled with blood. A duodenal ulcer and two gastric ulcers were found. All were chronic ulcers. He died on the fifth day from anuria.

CASE 5 (No. 175627, Louisville General Hospital).—G. D., a 43-year-old white man, was admitted, March 25, 1951, with a perforated anterior duodenal ulcer. He had had ulcer symptoms for 17 years. The anterior perforation was sutured. For five days he had an uneventful recovery. He then had several minor hemorrhages during the sixth through the eighth postoperative day, and on the ninth day had a severe hemorrhage, which produced clinical shock. At operation there was found in the posterior wall of the duodenum a second ulcer, which had penetrated the gastroduodenal artery. He was discharged from the hospital three and one-half weeks later.

COMMENT

In view of these experiences we are trying to find whether there is a possible causative relationship between surgical procedures and activation of peptic ulcers, or whether activation is an unrelated coincidence.

It has become generally accepted that duodenal ulcers are associated with hypersecretion; that this secretion has a high degree of acid and peptic power, and that the secretion occurs in the absence of normal stimuli. Because the secretion occurs in the absence of normal stimuli, it pours into the duodenum unneutralized by food or other material. It is well known that the ulcer patient does not do well when his stomach is empty for long periods of time, and medical regimens are based largely on attempts to keep some neutralizing substance in the stomach.

Knowing that patients who undergo major surgery usually eat little or nothing for periods of several days, and that their stomachs contain little or no neutralizing materials, we felt that if such patients secreted moderately or highly acid gastric juices during these periods, a causative relationship between major surgical procedures and activation of duodenal ulcers could be said to be demonstrated.

We are studying the postoperative gastric secretion in three types of patients: first, those with active ulcers; second, those with quiescent ulcers, and third, those with no evidence of ulcer. In this paper we shall deal only with the first type, that is, patients with active ulcers. Studies on the other groups are in progress.

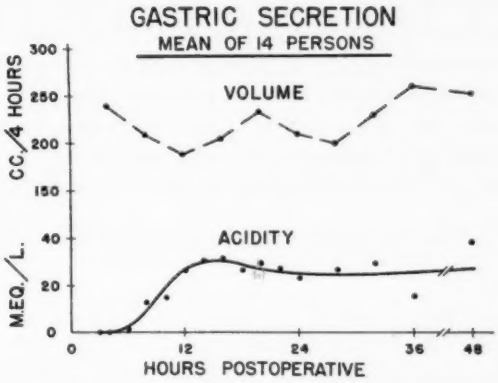
PATIENTS WITH ACTIVE ULCERS

We collected the gastric secretions from 11 patients during the first 24 hours after closure of perforations of anterior duodenal ulcers. The secretions were obtained by continuous suction and collected at 4-hour intervals for the 24 hours. The pH of specimens was measured by a pH meter, and the free acidity was determined from the pH, with use of curves which relate pH to activity of hydrogen ions. Comparisons of acidity as determined by pH with acidity as measured by colori-

metric titrations of colorless specimens shows the two methods to agree very closely over the entire range of pH of gastric juice. Nearly all specimens obtained by continuous suction are deeply stained with bile, and no attempt was made to correct the acidity for this contamination.

Uniformly, acidity increased from low levels at 4 hours after surgery to well-sustained hyperacidity levels at 8 to 12 hours (Chart).

We also determined the volume and acidity of gastric secretions during the second 12-hour period after operation in these 11 patients. Data obtained from secretions



Values represent the mean of 14 persons with peptic ulcer during the immediate postoperative period following closure of perforation. Graph of volume shows the quantity of secretion recovered by continuous suction during consecutive four-hour periods. Acidity curve is an interpolation of the mean values of free acidity.

TABLE 1.—*Free Acidity of 12-Hour Secretions in Milliequivalents per Liter (Clinical Units)**

	Controls	Postop. Patients
Mean	40.5	39.1
Standard deviation	19.7	21.0
Maximum	105.0	81.6
Minimum	2.4	5.1
No. of persons	38	11

* Control values were obtained from persons with duodenal ulcer before gastric surgery. Postoperative values were obtained during the second 12-hour period following closure of perforated duodenal ulcer.

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After suture of duodenal perforations, the concentration of acid in the gastric secretion frequently attained levels within 8 to 12 hours comparable to those found in patients with active duodenal ulcers (Table 1).

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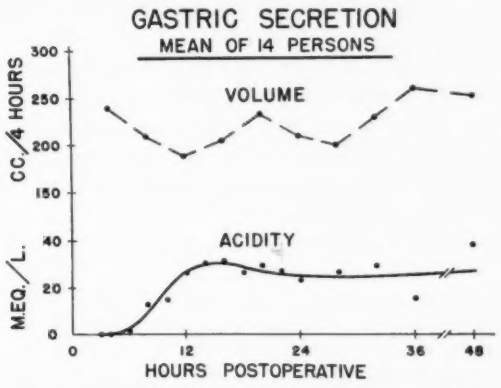

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regardless of the type of surgery, except, of course, after operations designed to lower gastric acidity. This we have found to be true in the one such patient we have been able to study so far. Thus, patients with active ulcers should be subject to increasing activity and to complications of their ulcers during their postoperative course because of the high acid concentrations of the gastric juice which have here been demonstrated to occur during the early postoperative starvation period.

We found smaller volumes in postoperative duodenorrhaphy patients than in preoperative duodenal ulcer patients.

However, the secretions of the preoperative group were collected by a trained, full-time research team, and the secretions of the duodenorrhaphy group were collected by the usual ward personnel of a charity hospital. It is entirely possible that, because of lack of attention to details by the ward personnel, the suction tubes were not always working, and the secretions were not completely aspirated.

In any case, however, the volume is of secondary importance, for there is little or no neutralizing material in the stomach during the postoperative period and the duodenum is subjected to whatever gastric juice is present in an unneutralized state.

TABLE 2.—*Volume of 12-Hour Secretions in Cubic Centimeters**

	Controls	Postop. Patients
Mean	1164	625
Standard deviation	521	225
Maximum	2580	1100
Minimum	384	250
No. of persons	38	11

* Control values were obtained as in Table 1.

Although the status of gastric secretion in an ulcer patient during the periods when the ulcer is quiescent as compared with secretion of normal individuals is not fully understood, the secretion of a given ulcer patient is higher when the ulcer is active than when it is quiescent.

We have no secretory data on our patients who were clinically quiescent before surgery and who bled in the postoperative period. As to whether the hemorrhages were due to coincidence, to an ulcer type of gastric secretion occurring in the postoperative period and unbuffered by food, or to a susceptible duodenal mucosa which was exposed to a normal type of gastric secretion in the postoperative starvation period, we are not prepared to say. We are now trying to get data on patients who are similar in that they have quiescent ulcers and are undergoing surgery for other conditions.

Hardy [1] and Gray and others [2] have published data which suggest a mechanism whereby gastric secretion could be increased by major surgical procedures and which would explain the cause of these complications.

1. Hardy, J. D.: The Adrenal Cortex and Postoperative Gastrointestinal Secretions: Clinical Significance of These Effects, Surgery **29**:517-522, 1951.

2. Gray, S. J.; Benson, J. A., Jr.; Reifenstein, R. W., and Spiro, H. M.: Chronic Stress and Peptic Ulcer: Effect of Corticotropin (ACTH) and Cortisone on Gastric Secretion, J. A. M. A. **147**:1529-1537, 1951.

Gray gave 100 to 150 mg. of corticotropin (ACTH) daily for three to four weeks to a series of gastrically normal patients and to one quiescent duodenal ulcer patient. He found gastric secretions greatly increased in volume and in acidity, and the most marked increase was in the quiescent duodenal ulcer patient. These increases occurred oftenest in the first week, but a few occurred only after three weeks.

Hardy studied adrenal activity by eosinophile counts in three patients after combined abdominoperineal resections of the rectum. There was a rise in adrenal activity in 24 hours with a return to normal within 48 to 72 hours. However, at present, there is no way to compare quantitatively the adrenal activity as measured by an eosinophile response as used by Hardy [1] and the amount of corticotropin and its effect on gastric secretion as reported by Gray.[2]

SUMMARY AND CONCLUSIONS

Four patients with quiescent peptic ulcers bled after various operations not related to the stomach.

One patient bled from a posterior ulcer nine days after repair of a perforation in the anterior duodenum.

Our studies of patients with active duodenal ulcers showed a return of gastric secretions within 8 to 12 hours to a level comparable to that found in active ulcer patients.

These data indicate that a patient with an active duodenal ulcer who undergoes surgery for other conditions may secrete highly acid gastric juice in the immediate postoperative period. The complications of hemorrhage or perforation are likely to develop during this period, and special attention should be devoted to this aspect of the postoperative care of such a patient.

DISCUSSION

DR. JOHN H. GRINDLAY, Rochester, Minn.: I am certain that if Dr. Dragstedt were here, he would like to comment on this study. I would like to comment only to underscore Dr. Drye's remarks.

A similar gastric hypersecretion often occurs in dogs. If any of you are ever guilty of performing surgery on dogs in order to carry on gastric secretion studies, you will observe this to be true for a brief period of time after operation. We suppose it is caused by tissue injury incident to the operation.

Certain states of malnutrition or deficiency will also cause gastric juice hypersecretion, and so will infection. We have learned that this is true in dogs. It is necessary to be aware of such factors in all studies in which the gastric secretion is measured before and after various types of gastroenteric anastomoses or exclusions of portions of the stomach or such procedures in dogs. When the study is reported, it should be stated how long an interval elapsed after an operation before measurements are begun. It may be true that some data published in the past are based on an abnormal situation in which measurements of gastric secretion were made when there was infection of a wound, or too early after operation, or when there was a nutritional deficiency.

DR. RUDOLF J. NOER, Louisville, Ky.: You may be interested in some of the background of the work which Dr. Drye has reported.

The paper which he gave covers but one in several series of studies now being carried on at the University of Louisville under a program started some years ago by Drs. Griswold and Schoen.

This is a cooperative study which is carried on jointly by the Departments of Medicine and Surgery, thus providing a much broader viewpoint than any approach to such problems would be in a single departmental study.

Dr. Schoen, whose name appears on this paper, is the none-too-common type of internist whom we sometimes refer to as a "surgical internist," by way of recognizing his appreciation of the values of surgical therapy.

These studies of gastric secretion, about some of which you have heard, were carried out under Dr. Schoen's direct supervision in the Institute for Medical Research, situated in a wing of the General Hospital, which is designed and equipped for careful physiological studies of patients admitted to that institution. The laboratory findings are, therefore, dependable and accurate—a thing unfortunately not always true of routine hospital laboratory examinations.

I am sure this particular study indicates that we should all be more alert to the possibilities of peptic ulcer complications during the early postoperative period.

The early rise in acidity is probably a factor which many of us have not fully appreciated, and one which I am sure we should all take cognizance of in planning the postoperative care of such patients.

DUODENAL OBSTRUCTION IN INFANTS AND CHILDREN

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OBSTRUCTION of the duodenum occurring in infants and children is almost invariably the result of congenital maldevelopment. The origin of the obstruction may be intrinsic or extrinsic. Intrinsic obstruction is usually caused by atresia and is therefore complete. However, incomplete intrinsic obstruction due to stenosis may also occur. Extrinsic obstruction is usually incomplete and is frequently accompanied by other anomalies. These accompanying anomalies may be malrotation of the colon, midgut volvulus, or both. Abnormalities in the second stage of intestinal rotation may account for the extrinsic duodenal obstruction, the malrotation of the colon, and the midgut volvulus.

The embryologic aspects of the conditions resulting in duodenal obstruction have been thoroughly and completely presented in the publications of Dott,[1] Ladd,[2] Wakefield and Mayo,[3] Gardner and Hart,[4] Webb and Wangensteen,[5] Haymond and Dragstedt,[6] and others. Further elaboration on this phase of the problem would be unnecessarily repetitious.

From the historical standpoint, it is worth remembering that only in comparatively recent years has the surgical treatment of congenital intestinal obstruction been attended by any degree of success.[7] The mortality following duodenal obstruction is still appreciable but can undoubtedly be lowered by earlier diagnosis and prompt institution of surgical treatment.

From the Surgical Service of the Children's Memorial Hospital.

Read at the Tenth Annual Meeting of the Central Surgical Association, Chicago, March 7, 1953.

1. Dott, N. M.: Anomalies of Intestinal Rotation: Their Embryological and Surgical Aspects, with Report of 5 Cases, Brit. J. Surg. **11**:251, 1923.

2. Ladd, W. E.: Congenital Obstruction of the Small Intestine, J. A. M. A. **101**:1453, 1933.

3. Wakefield, E. G., and Mayo, C. W.: Intestinal Obstruction Produced by Mesenteric Bands in Association with Failure of Intestinal Rotation, Arch. Surg. **33**:47, 1936.

4. Gardner, C. E., and Hart, D.: Anomalies of Intestinal Rotation as a Cause of Intestinal Obstruction: Report of 2 Personal Observations; Review of 103 Reported Cases, Arch. Surg. **29**:942, 1934.

5. Webb, C. H., and Wangensteen, O. H.: Congenital Intestinal Atresia, Am. J. Dis. Child. **41**:262, 1931.

6. Haymond, H. E., and Dragstedt, L. R.: Anomalies of Intestinal Rotation: Review of Literature with Report of 2 Cases, Surg., Gynec. & Obst. **53**:316, 1931.

7. (*a*) Glover, D. M., and Barry, F. M.: Intestinal Obstruction in the Newborn, Ann. Surg. **130**:480, 1949. (*b*) Potts, W. J.: Congenital Atresia of Intestine and Colon, Surg., Gynec. & Obst. **85**:14, 1947. (*c*) Webb and Wangensteen.[5]

The material forming the basis for this report was obtained from the records of 21 patients with duodenal obstruction who were admitted to the Children's Memorial Hospital during a seven-year period between Jan. 15, 1946, and Jan. 15, 1953. Because the majority of the patients were young infants, it was felt that an account of the experiences gained from their management would be of value. Only those patients in whom the principal ailment was duodenal obstruction were included. Some of these patients had an incidental nonstrangulating volvulus. When strangulating volvulus was the primary disorder, even though an associated incomplete duodenal obstruction was also present, the patients were not included.

AGE AND SEX

The ages of the patients ranged from 1 day to 5 years. Sixteen patients were 12 days of age or younger. The ages of the five patients more than 12 days old were 3 weeks, 2 months, 7 months, 14 months, and 5 years. There were seven patients with duodenal atresia varying in age from 1 to 5 days. Three of these patients were premature infants.

The sex distribution in the group was approximately equal, with 11 girls and 10 boys. However, all seven patients with duodenal atresia were girls.

CLINICAL MANIFESTATIONS

Patients with Duodenal Atresia.—Vomiting was the outstanding clinical feature. The vomiting was persistent and became progressively more frequent and severe as attempts at feeding were made. Grossly evident bile was present in the vomitus of six of the seven patients with atresia. In one patient either bile was absent from the vomitus or its presence was not recorded. The initial vomitus of two patients contained bright red blood. This was noted in the first 2 or 3 episodes of vomiting and then disappeared, to be followed by the usual biliary regurgitation.

The stools were either absent or only a few were passed after birth. They were usually grayish green in color, mucoid, and small in amount. This was in marked contrast to the tarry appearance of normal meconium.

Physical examination often disclosed evidences of weight loss, dehydration, and jaundice. The jaundice was not directly related to the duodenal obstruction in any patient but was the usual icterus of the newborn infant. Distention of the upper abdomen was not observed; in fact, the abdomen may be scaphoid in appearance in some patients.

Laboratory procedures revealed the usual changes expected in patients who were dehydrated and anemic. No diagnostic aid was obtained from either the physical or the laboratory examinations.

A brief case history which is typical of duodenal atresia illustrates the clinical manifestations.

Case 4.—J. F., a white girl, 3 days of age, was admitted to the hospital on April 16, 1948. On the second day of life, vomiting of brownish green material occurred and continued after each feeding, becoming progressively more intense. One stool had been passed since birth.

Roentgenograms taken prior to admission disclosed air in the stomach and none in the intestines.

Physical examination disclosed a small dehydrated infant weighing 4 lb. 2 oz. (1.8 kg.). Slight icterus was present. There were no other remarkable physical findings. Postadmission roentgenograms showed two fluid-air levels, one representing the stomach, the other the duodenum with no air distal to the duodenum.

At operation on April 17, 1948, an atresia just beyond the duodenal papilla was noted. A jejunal loop was carried over the colon, and an anastomosis to the proximal dilated loop of duodenum was established. No other atresia could be demonstrated in the intestinal tract.

Incomplete Duodenal Obstruction.—Nine patients had symptoms so severe that treatment was carried out before their 12th day of life. In these patients the clinical manifestations were very similar to those occurring in atresia. Thus, persistent vomiting was present in all cases. Bile was present in the vomitus in eight patients, and bright red blood was observed in two patients.

The stools were more frequent in number than those in atresia and were darker in color. Normal meconium stools were passed in several instances. The physical findings were similar to those in atresia, and the differentiation between atresia and nearly complete extrinsic obstruction was made either by roentgenography or at operation.

In the five older patients with partial obstruction the symptoms were not immediately recognized as being due to duodenal obstruction. The following two abstracts typify the clinical manifestations in this group.

CASE 5.—E. C., a Negro girl, 14 months of age, was admitted to the hospital on May 12, 1948. The mother stated that vomiting had been intermittently present since birth but had never been severe until the child was 6 months of age. At that time an attack occurred which lasted one week and was characterized by projectile vomiting. A physician examined the infant and stated that an obstruction was present which might require surgical intervention. However, the attack gradually subsided, and little difficulty was subsequently experienced, although at no time since birth had more than three or four days elapsed without the occurrence of vomiting. Constipation was also a constant symptom.

On May 8, 1948, she began to vomit three or four times daily immediately after eating. The vomitus was either yellowish green or definitely green in color.

On May 11, 1948, the mother observed large waves in the upper abdomen passing from right to left. No stools had been passed for several days before the patient's entrance to the hospital.

Physical examination disclosed a dextrocardia. The abdomen was somewhat protuberant, with visible peristaltic waves passing from right to left. The liver was outlined by percussion in the left upper abdomen.

Roentgenograms revealed duodenal obstruction and situs inversus of the abdominal viscera. A chest film and the electrocardiogram disclosed dextrocardia.

At operation the situs inversus was evident, and bands crossing the duodenum causing the obstruction were divided. Nonrotation of the colon and absence of the spleen were also observed.

One week after the operation it was necessary, because of a recurrence of the obstruction due to adhesions about the duodenum, to operate for the second time. At this operation a gastrojejunostomy was done, and recovery which was satisfactory followed.

CASE 20.—C. H., a white boy, 7 months of age, was admitted to the hospital on July 6, 1952. He had been a "feeding problem" since birth. Recurrent attacks of vomiting and loose stools had been frequent. Failure to gain weight was evident. He had been examined by many physicians, and various changes in the feeding formula had been tried, without beneficial effects. Several different diagnoses, including celiac disease and intestinal allergy, had been made.

Physical examination showed a small poorly nourished underweight infant with a protuberant abdomen. No abdominal masses were palpated, and there were no other abnormalities.

Roentgenographic study showed a very large stomach and duodenal bulb. The barium met an obstruction in the second portion of the duodenum, beyond which no barium passed for 10 minutes. A film taken one hour after the barium was administered showed only a small amount in the small intestine.

At operation on July 7, 1952, the duodenum was enlarged to three times normal size to a point 2.5 cm. distal to the duodenal papilla. A membrane or diaphragm inside the duodenum could be felt by external palpation. The duodenal wall was opened longitudinally, and the membrane which occluded seven-eighths of the lumen was found. The membrane was cut, and the edges of the mucosa were turned in with silk sutures. The duodenum was then closed transversely and the abdominal incision sutured.

Postoperative recovery was prompt and complete.

These two patients present examples of incomplete duodenal obstruction in which the symptoms are often thought to be due to other causes.

Treatment by formula changes, laxatives, and other medical measures is often continued for indefinite periods of time until the true cause of the vomiting attacks is discovered.

ROENTGENOGRAPHY

The roentgenographic examinations were of paramount importance in the diagnosis. In patients with atresia two fluid-air pockets were seen (Fig. 1). One pocket represented the dilated stomach, the other the dilated proximal duodenum. No air shadows distal to the dilated duodenum were present. These films were best taken in the upright position. In six of the seven patients with atresia the roentgenograms were typical. In the remaining patient (Case 13), who had a tracheoesophageal fistula, air was observed in the stomach, but none was seen in the small intestine. The significance of this observation was not appreciated at the time it was discovered, and the duodenal atresia was later found at necropsy.

In partial obstructions the stomach and proximal duodenum may be dilated, but it was often advisable to administer a thin barium mixture orally to demonstrate the obstruction. The narrowed duodenal area and marked delay in gastric emptying was then apparent. Ten patients were shown to have duodenal obstruction by this method. After the diagnosis was evident, the barium mixture was aspirated (Fig. 2).

More recently, iodized oil U. S. P. (Lipiodol) has been substituted for barium. If it is vomited and aspirated, no harm should follow. The dangers of barium aspiration have been stressed repeatedly, although no harm follows its use if it is withdrawn from the stomach after the obstruction is demonstrated.[8]

Because of the frequent coexistence of malrotation of the colon and duodenal obstruction, a barium enema is often administered. This may reveal the cecum in the right or left upper abdomen (Fig. 3). Demonstration of this particular anomaly was successful in four patients. In one patient the cecum was in the left upper abdomen, in another in the right upper abdomen, and in two patients a situs inversus of the colon with abnormal rotation was disclosed. The remaining patients did not undergo colon roentgenography.

For an additional patient not included in the series, a roentgenographic diagnosis of an incomplete duodenal obstruction was made. At operation there were no signs of obstruction or other abdominal abnormalities, except a few filmy adhesions between the duodenum and ascending colon. Postoperatively, persistent biliary vomiting occurred. Repeated roentgenograms showed no obstruction in the gastro-

8. (*a*) Ladd, W. E., and Gross, R. E.: Abdominal Surgery in Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1947. (*b*) Ladd.[2] (*c*) Potts.[7b]

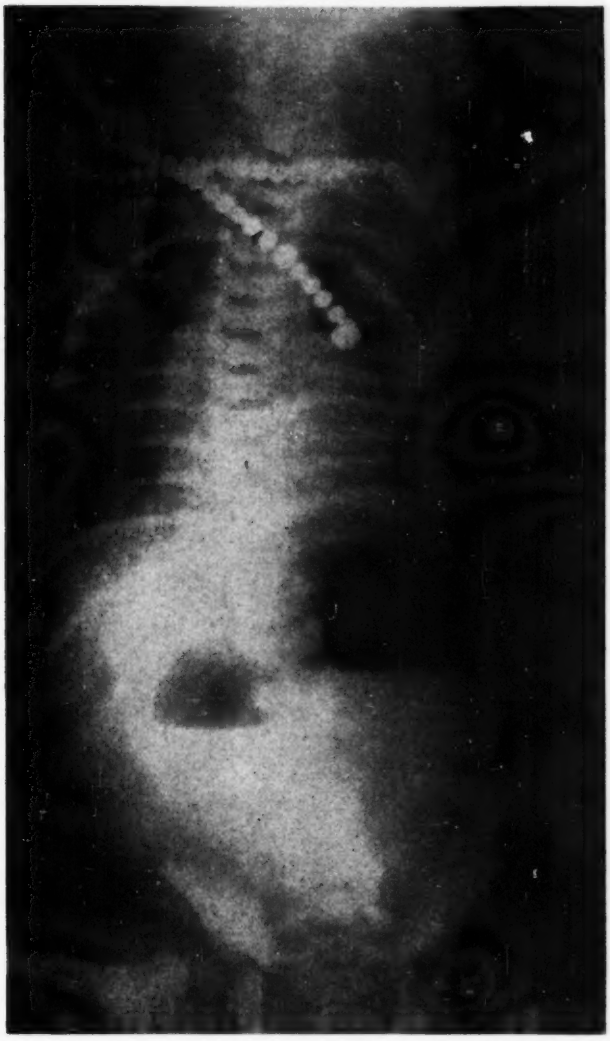

Fig. 1.—Typical roentgenogram of duodenal atresia showing fluid-air bubbles in stomach and duodenum. Film is taken in the upright position. Note absence of air distal to duodenum.

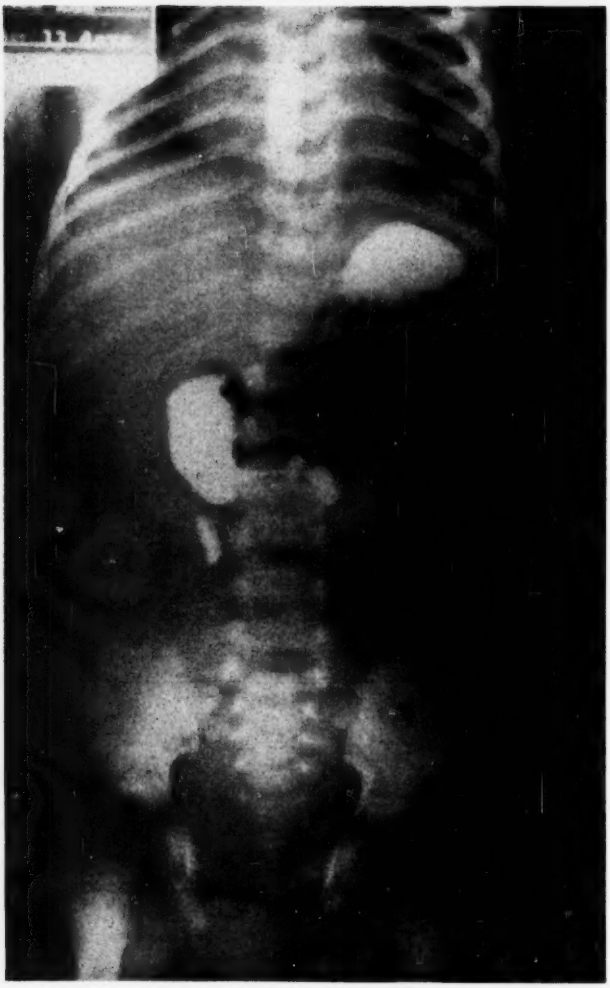

Fig. 2.—Roentgenogram after administration of opaque medium in incomplete duodenal obstruction. Note duodenal narrowing and small amount of opaque material distal to duodenum.

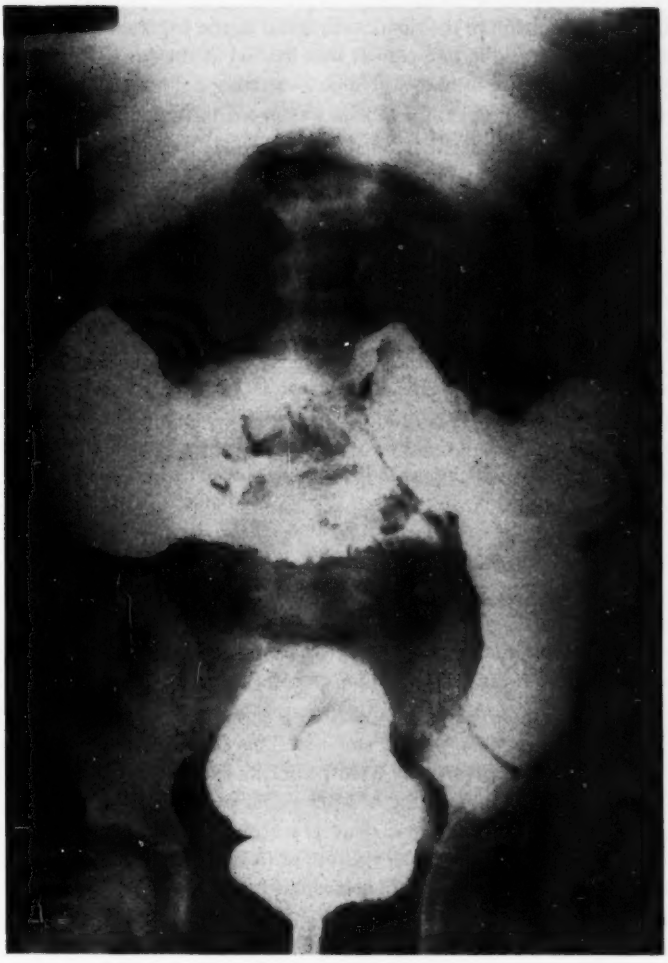

Fig. 3.—Malrotation of colon, with cecum in upper right abdomen.

intestinal tract. Finally, after one month of hospital management the patient was well enough to be discharged. Feeding problem was the final unsatisfactory diagnosis.

CAUSE OF OBSTRUCTION

In seven patients duodenal atresia was present. In five patients the obstruction was in the second portion of the duodenum distal to the papilla. All of these patients vomited bile. The atresia in one patient was located at the junction of the first and second portions of the duodenum, and biliary vomiting did not occur. In the remaining patient, who did vomit bile, the atresia was in the third portion of the duodenum.

Twelve patients had partial duodenal obstructions varying in severity because of adhesive bands crossing the duodenum, usually in the second portion. These bands often extended from the posterolateral abdominal wall to the cecum, holding it in the right upper abdomen, producing a malrotation.

In one patient (Case 3) a stricture of the duodenum 2 cm. distal to the pylorus was the cause of obstruction. In the remaining patient (Case 20) the obstruction was due to a membrane occluding seven-eighths of the lumen. This membrane was located 2.5 cm. distal to the duodenal papilla.

One of the 12 patients with adhesive bands (Case 19) also had a partially obstructing membrane in the second portion of the duodenum. At the first operation the bands were divided. Five days later a second operation was necessary to circumvent the membrane which was still producing obstruction.

DIAGNOSIS

The diagnosis of duodenal obstruction is based upon the history of repeated vomiting, which usually contains bile, and typical roentgenographic findings. In duodenal atresia the diagnosis may be readily made. In partial obstructions, particularly in older children, with periodic repeated attacks of biliary vomiting and constipation, reliance must be placed almost entirely on the roentgenograms.

The most important differential diagnosis must be made between duodenal obstruction and hypertrophic pyloric stenosis. This is not ordinarily difficult, since infants with pyloric stenosis usually have projectile vomiting; the vomitus contains no bile, and a mass representing the hypertrophied pylorus is palpable in almost all cases. Only one patient with pyloric stenosis was seen who vomited bile repeatedly. At operation the ductus choledochus was found to have an anomalous insertion into the pyloric antrum proximal to the hypertrophied area.

Intestinal obstructions in the jejunum and ileum can usually be differentiated readily by the scout film of the abdomen.

ASSOCIATED ABNORMALITIES

Because of the frequent occurrence of associated abnormalities, the surgeon must be prepared to encounter them. Reduction of an accompanying volvulus and correction of a malrotation of the colon must be done when these are present.

In all cases of atresia the collapsed intestine beyond the obstructed point should be tested for patency. In Case 12 a second atresia was demonstrated in the sigmoid colon.

All of the associated abnormalities encountered are listed in Table 1. In Case 5 nonrotation of the colon, situs inversus, and absence of the spleen were observed. This patient has previously been reported in detail.[9]

When malrotation of the colon was found, it was due to the cecum being held in the upper right or left abdomen by the adhesions which were causing the duodenal obstruction. The division of these adhesions accomplished relief of the duodenal obstruction, as well as correction of the malrotation. Actually the cecum tends to fall into the left lower quadrant or lower central abdomen after the adhesions are divided. This results in a nonrotation of the colon, which is ordinarily asymptomatic. In the nine patients of the series in whom malrotations of the colon were corrected, there were no postoperative symptoms referable to the colon.

OPERATIONS

An operation which circumvented the obstruction was done in six of the seven patients with atresia. Duodenojejunostomy was performed in four patients. In Case 1 a gastroduodenostomy was utilized, and in Case 8 an anterior gastrojejunostomy was chosen. A sigmoidosigmoidostomy, in addition to the duodenojejunostomy, was necessary in Case 12. Because of cyanosis due to laryngeal edema and inflammation, a preliminary tracheotomy was indicated in Case 10.

The choice of the operative procedure in duodenal atresia depends somewhat on the level of the obstruction. If the atresia is in the proximal duodenum, a gastrojejunostomy may be performed. If the obstruction is in the second portion, as it usually is, a duodenojejunostomy is the best choice. In all cases of atresia 0.9% saline solution should be injected into the collapsed distal intestine to test for multiple atresias. This injection also distends the collapsed bowel, making the anastomosis easier to perform and helping to facilitate passage of the bowel contents after the operation. Any type of enterostomy with external drainage is best avoided if possible.[10]

In all of these patients the anastomosis performed for the relief of the atresia remained patent and intact, with no leakage or breakdown of the suture lines.

In the incomplete obstructions five patients required simple division of the adhesive bands. This was sufficient to relieve the obstruction and correct any coexisting malrotation of the colon. Four patients with associated volvulus had reduction of the volvulus and division of the adhesive bands. In Case 20 the duodenal wall was opened longitudinally at the site of the incompletely obstructing membrane. The membrane was partially removed, and the duodenum was closed transversely to increase the size of its lumen.

Five patients required a second operation, because it was thought that the obstruction was not sufficiently corrected by the first procedure. In Case 3 the second operation, a catheter jejunostomy, was unsuccessful. Jejunostomies are poorly tolerated by infants.[10] The patient of Case 18 was discharged from the hospital after the first operation and readmitted eight days later with persistent biliary vomiting, fever, and abdominal distention. A second operation disclosed no obstruction. After

9. Fox, P. F., and Crawford, O. W.: Duodenal Obstruction: Situs Inversus and Nonrotation of the Colon, Surgery **27**:896, 1950.

10. (*a*) Morton, J. J., and Jones, T. B.: Obstructions About the Mesentery in Infants, Ann. Surg. **104**:864, 1936. (*b*) Ladd and Gross.[8a]

TABLE 1.—*Patients with Duodenal Obstruction**

Case No.	Identification	Date of Admission	Age	Sex	Cause of Obstruction	Associated Findings	Operation	Result
1	J. B.	5/29/46	3 days	F	Complete atresia of duodenum	Adhesions crossing duodenum; prematurity	Gastroduodenostomy	Death
2	D. U.	5/23/47	4 days	M	Band of adhesions crossing 2nd part of duodenum	Cecum held against duodenum in upper right abdomen	Adhesions divided	Complete recovery
3	H. B.	1/ 5/48	2 mo.	M	Duodenal stricture 2 cm. distal to pylorus	None	1st, duodenum cut longitudinally at site of stricture and closed transversely; 2nd, catheter jejunostomy	Death
4	J. F.	4/16/48	3 days	F	Complete atresia distal to ampulla	None	Duodenojejunostomy	Complete recovery
5	E. C.	5/12/48	14 mo.	F	Band of adhesions crossing 2nd part of duodenum	Situs inversus; complete nonrotation of colon; absence of spleen	1st, adhesions divided; 2nd, gastrojejunostomy	Complete recovery
6	J. R.	8/ 2/48	5 days	F	Complete atresia of 3rd portion of duodenum	None	Duodenojejunostomy	Death
7	D. K.	9/ 5/48	7 days	M	Band of adhesions crossing 3rd portion of duodenum	Malrotation of colon; cecum in right upper abdomen	Adhesions divided	Complete recovery
8	B. S.	1/ 9/49	4 days	F	Complete atresia of 2nd part of duodenum	Prematurity; wt. 3 lb. 2 oz.	Gastrojejunostomy	Death
9	C. D.	8/ 8/49	5 yr.	F	Band of adhesions crossing 3rd portion of duodenum	Malrotation of colon with nonstrangulating volvulus of cecum and ascending, transverse, and part of descending colon	Reduction of volvulus; division of adhesions	Complete recovery
10	J. M.	10/31/49	1 day	F	Complete atresia of duodenum 5 cm. distal to pylorus	Imperforate anus; rectovaginal fistula	Tracheotomy and duodenojejunostomy	Death

11	J. V.	4/13/50	12 days	M	Band of adhesions crossing 2nd part of duodenum	Malrotation of colon with cecum in right upper abdomen; non-strangulating small intestinal volvulus	Volvulus reduced; adhesions divided	Complete recovery
12	J. C.	5/ 3/50	2 days	F	Complete atresia of 2nd portion of duodenum	Complete atresia, sigmoid colon; malrotation of colon	Duodenojejunostomy; sigmoid-osigmoidostomy	Death
13	A. J.	7/ 6/50	2 days	F	Complete atresia at junction of 1st and 2nd portions of duodenum	Tracheoesophageal fistula	Repair of tracheoesophageal fistula	Death
14	L. B.	12/ 1/50	4 days	F	Band of adhesions crossing 2nd portion of duodenum	Malrotation of colon with cecum in right upper abdomen	Adhesions divided	Complete recovery
15	J. C.	4/25/51	11 days	M	Band of adhesions crossing 2nd portion of duodenum	None	Adhesions divided	Complete recovery
16	T. Z.	6/17/51	2 days	M	Band of adhesions crossing 3rd portion of duodenum	Malrotation of colon with cecum in upper right abdomen; non-strangulating volvulus of small intestine	Volvulus corrected; adhesions divided	Complete recovery
17	J. N.	12/ 6/51	6 days	M	Band of adhesions crossing 2nd portion of duodenum	Malrotation of colon with cecum in left upper abdomen	Adhesions divided	Complete recovery
18	G. C.	12/28/51	3 wk.	M	Band of adhesions crossing 2nd portion of duodenum	Pylorus on left side of abdomen; spleen in midline below liver; cecum on left; sigmoid on right	1st, adhesions divided; 2nd, exploration (no obstruction found)	Complete recovery
19	M. P.	4/18/52	7 days	F	Band of adhesions crossing 2nd portion of duodenum with membrane in lumen	Malrotation of colon; cecum in right upper abdomen	1st, adhesions divided; 2nd, obstructing web with small opening in it circumvented by duodenoduodenostomy	Complete recovery
20	C. H.	7/ 6/42	7 mo.	M	Membrane in 2nd portion obstructing ⅞ of lumen 2.5 cm. distal to papilla	None	Duodenal wall opened longitudinally; membrane cut; wall closed transversely	Complete recovery
21	G. M.	1/11/53	11 days	M	Band of adhesions crossing 2nd portion of duodenum	Malrotation of colon with cecum in right upper quadrant; midgut volvulus	1st, adhesions divided; 2nd, secondary adhesions divided	Recovery (too recent to evaluate fully)

* Cases are numbered chronologically.

the second operation a chest film revealed a pneumonic process. Satisfactory recovery occurred after the pneumonia was treated. A secondary obstruction due to the formation of adhesions was found in Cases 5 and 21. In Case 19 an obstructing membrane which was not discovered at the first operation was circumvented by duodenoduodenostomy.

RESULTS

Seven deaths occurred in the series, resulting in a mortality rate of 33.3%. Of the seven patients with atresia, one patient recovered. This distressingly high mortaity of 85% is due, at least to a considerable extent, to the coexisting congenital defects. Necropsies were performed on all patients who died, and the findings are summarized in Table 2.

Only one death occurred in the 14 patients with incomplete obstructions, producing a mortality rate of 7.1%. Although five of the patients underwent second

TABLE 2.—*Necropsy Findings*

Case No.	Findings at Necropsy
1	Atresia of duodenum; congestive heart failure; prematurity
3	Pulmonary atelectasis; patent foramen ovale and ductus arteriosus
6	Duodenal atresia; bronchopneumonia; atelectasis
8	Duodenal atresia; pulmonary hemorrhages and congestion; prematurity; patent foramen ovale
10	Duodenal atresia; imperforate anus and rectovaginal fistula; multiple anomalies of heart and genitourinary tract
12	Atresia of duodenum and sigmoid; malrotation of colon; prematurity; bronchopneumonia
13	Unsuspected atresia of duodenum; mediastinal abscess; leakage at site of esophageal anastomosis

operations, recovery was satisfactory, except in Case 3. All the patients with partial obstructions requiring one operation recovered fully. Some of the patients operated upon recently have only a short follow-up record.

COMMENT

The vomiting of duodenal atresia is usually biliary, because the obstruction is distal to the duodenal papilla. According to Morton and Jones,[10a] the presence of blood in the vomitus is considered pathognomonic of duodenal atresia or stenosis. Two patients with atresia in this series vomited blood. Any persistent vomiting occurring in a newborn infant, whether or not bile or blood is present, should be investigated by roentgenography.

The typical stools in duodenal atresia are small in volume, grayish green, and mucoid. Ladd and Gross [8a] observed that in some instances they may resemble meconium. For this reason the Farber test is useful, because it will differentiate true meconium from stools resembling meconium. The test detects the presence of cornified epithelial cells which come from the desquamated skin of the fetus.[11] If these cells are absent from the stools, an atresia is present.

11. Farber, S.: Congenital Atresia of the Alimentary Tract: Diagnosis by Microscopic Examination of the Meconium, J. A. M. A. **100**:1753, 1933.

Morton and Jones [10a] pointed out that bile in the vomitus is not reliable in localizing the obstruction, because accessory bile ducts may enter the intestine above and below the obstruction. Therefore, bile may also be found in the stools. In addition, they stated that secretion of bile begins about the third month, but the obstruction may not develop until much later. The first bowel movements after birth would then contain bile which reached the lower intestine before the obstruction was established.

The results of the surgical treatment of duodenal atresia are often discouraging. Webb and Wangensteen [5] stated that many authorities regard intestinal atresia as invariably fatal. Isolated reported instances of successful surgical treatment have been reported for many years, however, and in recent years results have been better. Although the mortality is still high, reports by Madding, Everhart, and Heath [12]; Morton and Jones [10a]; Glover and Barry [7a]; Ladd [2]; Potts,[7b] and others indicate that more survivals may be expected than in previous years. Earlier diagnosis and the preoperative correction of dehydration, electrolyte imbalance, and anemia are important factors influencing the results. Prompt surgical intervention, better anesthesia, and improved postoperative care also deserve emphasis. These measures, as carried out in this hospital, have been more fully discussed by Potts.[7b]

In incomplete duodenal obstruction the nine patients who were operated upon before the age of 12 days presented essentially the same problems as the patients with atresia. The outlook for these patients is much better, because the obstruction is not complete and some ingested material may reach the intestinal tract for digestion and absorption. The magnitude of the surgical procedure is usually not as great, because an anastomosis is not required. These nine patients, whose obstructions were due to extrinsic bands or incomplete septa in the lumen, survived, and their recovery was satisfactory.

The five older patients with incomplete obstruction had symptoms since birth, but in all instances the correct diagnosis was not made at once. In Case 3 the obstruction was due to a duodenal stricture, but it was thought at first to be due to pyloric stenosis. A septum occluding seven-eighths of the duodenal lumen produced the obstruction in Case 20. Neither of the patients had an associated malrotation or volvulus. In Cases 5, 9, and 18 the associated anomalies included complete and partial situs inversus, volvulus of the colon, absence of the spleen, and abnormal rotation of the colon. These patients had symptoms for varying periods of time which were considered to be caused by celiac disease, feeding problems, or other reasons. It is characteristic of these older patients that they may continue for months or years with periodic attacks of biliary vomiting, abdominal pain, distention, and constipation, without a correct diagnosis being made until roentgenographic examination is performed. The publications by Haymond and Dragstedt,[6] Gardner and Hart,[4] Ladd,[2] Judd and White,[13] and Wakefield and Mayo [3] include a number of patients of this type.

SUMMARY AND CONCLUSIONS

Twenty-one patients with duodenal obstruction were treated during a seven-year period between Jan. 15, 1946, and Jan. 15, 1953.

12. Madding, G. F.; Everhart, M. W., and Heath, J.: Congenital Duodenal Atresia with Malrotation of the Intestine: Case Successfully Treated by Duodenojejunostomy, Ann. Surg. **131**:433, 1950.

13. Judd, E. S., and White, R. B.: Congenital Anomalies of the Duodenum with Obstruction at the Duodenojejunal Angle, Ann. Surg. **89**:1, 1929.

The most important features in the diagnosis were the occurrence of repeated biliary vomiting and characteristic roentgenographic findings.

The mortality rate for the entire series was 33.3%, with a mortality following duodenal atresia approximately 12 times as great as that following incomplete duodenal obstruction.

Coexisting congenital defects contribute to the mortality rate and to the difficulties encountered in the management of these patients.

DISCUSSION

DR. DONALD M. GLOVER, Cleveland: I would just like to emphasize two points that Dr. Fox has well made in his presentation on duodenal obstruction.

The first is the importance of vomiting in the newborn infant, especially when that vomitus contains bile. If this one simple symptom is recognized early and operation is done early, the very high mortality rate, which you saw and which is commonly observed by all of us, can be reduced greatly, because the obvious depletion in fluid balance in the newborn infant, often premature, has very significant bearing upon the mortality. It seems to be difficult to a significant degree to impress obstetricians and pediatricians with this fact, because we are constantly seeing these babies too late to have a good opportunity for repair that is successful.

The second point has to do with the multiple anomalies that are commonly present. Dr. Fox well stated that it is important to demonstrate continuity in the rest of the gastrointestinal tract after repairing the obvious abnormality.

I happened to have seen two significant cases confirming this in the last three weeks. One was duodenal stenosis due to volvulus and malrotation, which unfortunately was discovered late, and with pneumoperitoneum from an obvious perforation of viscus somewhere above it, which was discovered at operation. With release of the volvulus, we found on further exploration that there was a rent in the gastric wall about 5 cm. in length along the greater curvature of the stomach. This is a very rare complication, presumably in this instance secondary to the duodenal obstruction due to the volvulus. This patient died.

The second case, which we saw two weeks ago, is also illustrative. It was a case of volvulus with malrotation, with obstruction at the duodenojejunal junction, which we thought was entirely due to the obstruction at first, but on furher exploration we found there was also complete duodenal atresia at the third part of the duodenum, with separation of about 5 cm. between the blind end of the duodenum and the jejunum. In spite of the fact that this condition was not recognized until seven days after operation, an anastomosis was done, and the baby was still all right at the time we left Cleveland.

DR. ANGUS D. MCLACHLIN, London, Ont., Canada: I wish to reiterate what Dr. Fox and Dr. Glover have said about diagnosis. Newborn babies that vomit bile without the stomach being distended and do not pass curd should be suspect. In our area, one practitioner discovered two of these cases. A flat plate of the abdomen reveals the characteristic distention of the stomach and duodenum.

I wish to limit my remarks to complete atresia of the duodenum requiring anastomosis. We have had four of these cases, and I am almost afraid to say that all four patients survived.

The first 2 patients almost died. Lessons learned certainly helped with the third and fourth patients. These children now range from 6 months to 5 years of age, and all are making good progress. It is unusual, of course, that these children all had single defects, which at present seem compatible with normal life. Beyond the occurrence of bilateral inguinal herniae in one child, no other abnormalities have appeared.

The most important step in the technique seemed the formation of an opening of adequate size between the grossly distended duodenum and the collapsed jejunum. An initial distention of the jejunum may be accomplished by injection of air through a fine needle. In a duodenojejunal anastomosis, the essential step, of course, is the opening into the distal loop of jejunum. If this part of the anastomosis is carried out with a No. 14 catheter into the distal loop, the size of the anastomosis can be preserved while the corner is being turned. When a good opening has been obtained, the catheter can be withdrawn and the anastomosis completed at the entering loop, where size is not so important. Anastomoses have been done with one layer of fine non-

absorbable interrupted sutures. In the last two patients a No. 8 rubber catheter inserted through the nose was passed through the stomach and duodenum and led down into the distal loop of jejunum before the anastomosis was closed. This allowed early feeding into the distal loop.

The upper jejunum is of good texture in the newborn infant and very suitable for suture if it can be got up to an adequate size. We have certainly not had results as good as this in dealing with atresias lower down in the small bowel.

DR. EDWIN MILLER, Chicago: I didn't intend to say anything in discussion, but, in view of the figures presented by Dr. Fox, I thought I might just mention the fact that we have had experience with 11 atresias of the duodenum, with seven successful results. In atresia of the lower ileum, of which we have had experience with 25, we have only had two successful results.

DR. THOMAS C. MOORE, Muncie, Ind.: I would like to congratulate Dr. Fox on his fine presentation and would simply like to mention our experience at the Indiana University Medical Center, where I have just completed a study of 42 cases of stenosis and atresia of the small intestine.

The obstruction was limited to the duodenum in 25 of the cases. Additional congenital malformations were encountered in 53% of the entire group and in 45% of the duodenal cases. Esophageal atresia with tracheoesophageal fistula was found. Three patients had imperforate anus. In one patient we found an annular pancreas, an anomaly which should be considered in the differential diagnosis of neonatal duodenal obstruction. It is also of interest that 30% of our patients were premature infants.

There is an additional problem to be faced in dealing with these patients, particularly those who survive operative correction of the obstruction. It appears that there is a relatively high incidence of accompanying mental deficiency. Dr. Thomas Lanman, discussing a paper of Dr. Glover a few years ago, remarked that of 17 patients surviving operation for duodenal atresia at the Children's Hospital, Boston, 6 were found to be mentally defective, 4 of them being mongolian idiots. I think that it is of importance that these associated factors be borne in mind in our over-all evaluation of this problem.

In the last 15 years, 14 of our patients with duodenal stenosis or atresia have been operated upon, with 12 recoveries.

DR. PAUL F. FOX, Chicago: I wish to thank the discussants, and I am very sorry our results with duodenal atresia aren't better.

I wanted to mention one thing regarding the partial obstructions. After the malrotation is corrected and the adhesions are divided, one still must make sure that no partial intrinsic obstruction exists.

We had one patient who had a septum obstructing seven-eighths of the duodenal lumen, and after the initial operation was done—dividing the adhesions and correcting the malrotation —it required a secondary operation to correct the septal obstruction.

Case Reports

GASTROJEJUNAL ULCERS IN CHILDREN

JAMES M. MARSHALL, M.D.
PASADENA, CALIF.

THE CHIEF reason that gastrojejunal ulcer is so rarely seen in children is that so few children have gastrojejunostomies. Since the advent of the Ramstedt pyloroplasty for hypertrophic pyloric stenosis, gastrojejunostomy has been done mostly in infants with certain types of congenital atresia of the duodenum.

It is becoming increasingly evident that gastric and duodenal ulcers are commoner in children than was previously supposed. Proctor,[1] in 1925, found only 2 children with ulcer out of 8,260 patients with peptic ulcer at the Mayo Clinic. Yet of 1,000 consecutive patients with gastric ulcer, he found 16 with symptoms dating from childhood, and of 1,000 patients with duodenal ulcer, 26 had symptoms from childhood. Bird, Limper, and Mayer [2] were able to collect 120 cases of gastric and duodenal ulcers in children in a comprehensive review in 1941. Donovan and Santulli [3] found 10 cases of gastric and duodenal ulcer at New York Babies Hospital in a 15-year period through 1944. Strode,[4] in 1933, reported the only case of gastrojejunal ulcer in a child, proved at operation, that I have been able to find. McAleese and Sieber,[5] in reporting 16 cases of peptic ulcer encountered in 65,000 admissions at Children's Hospital of Pittsburgh, found 2 cases of marginal ulcer in children who had previously had gastrojejunostomy for duodenal ulcer. The diagnosis was apparently made by x-ray, and both patients had been given medical management at the time of the report.

REPORT OF A CASE

It is thought that the following case is worthy of report because of its extreme rarity and because of some unusual clinical features presented.

An 11-year-old girl was first seen on June 6, 1952, with a sudden massive gastrointestinal hemorrhage. Inquiry revealed the fact that when she was 4 days old gastrojejunostomy for complete duodenal atresia had been performed elsewhere. After this operation the child had been perfectly well in all respects until a few hours before admission, when she suddenly felt faint, and shortly afterward she passed several tarry stools. There had been no pain and no vomiting.

Examination revealed a well-nourished white girl with marked pallor and in moderate shock. The skin was cold and moist, the blood pressure 90/60, and the pulse rate 110 beats a minute. The abdomen was soft, peristalsis was audible; there was no tenderness and no palpable

1. Proctor, O. S.: Peptic Ulcer in Childhood, Surg., Gynec. & Obst. **41**:63 (July) 1925.

2. Bird, C. E.: Limper, M. A., and Mayer, J. M.: Surgery in Peptic Ulceration of Stomach and Duodenum in Infants and Children, Ann. Surg. **114**:526 (Oct.) 1941.

3. Donovan, E. J., and Santulli, T. V.: Gastric and Duodenal Ulcers in Infancy and in Childhood, Am. J. Dis. Child. **69**:176 (March) 1945.

4. Strode, J. E.: Gastro-Jejunal Ulcer in Childhood, Am. J. Surg. **21**:240 (Aug.) 1933.

5. McAleese, J. J., and Sieber, W. K.: The Surgical Problem Presented by Peptic Ulcer of the Stomach and Duodenum in Infancy and Childhood, Ann. Surg. **137**:334 (March) 1953.

organs or masses. A firmly healed 10 cm. upper right rectus surgical scar was present. Findings on rectal examination were negative except for the recovery of bloody stool. The blood count showed 5.9 gm. (35%) of hemoglobin per 100 cc., 1,940,000 erythrocytes, and 7,300 leucocytes, with a normal differential count. Whole blood, 500 cc., was given. Eight hours later the blood count showed 4.5 gm. (27%) of hemoglobin per 100 cc., and 1,630,000 red cells. A total of 1,500 cc. more blood was given during the next three days. The bleeding stopped promptly, and she improved rapidly.

X-ray studies were made 10 days after admission and repeated twice during the succeeding seven months. These x-rays revealed a functioning gastrojejunostomy with some delay in emptying but no definite evidence of a stomal ulcer. The duodenum filled promptly and was dilated to a diameter of 6 cm. until the terminal portion of the transverse duodenum, where it ended blindly. A moderate amount of barium remained in the duodenum and in the stomach three hours after ingestion. Roentgenographic examinations of the colon and chest revealed no abnormalities.

The patient left the hospital June 16, at which time the blood count showed 14.2 gm. (84%) of hemoglobin per 100 cc., and 4,600,000 erythrocytes. She was given a medical ulcer regimen. She remained well in all respects for six months and then was readmitted on Dec. 27., with weakness and tarry stools of two days' duration. Examination of the blood revealed 9.1 gm. (55%) of hemoglobin per 100 cc., and 3,250,000 erythrocytes. In two days 1,000 cc. of blood was given; the gross bleeding stopped, and she improved rapidly. Operation was advised but was postponed because of a serious operation upon another member of the family.

The child remained well for about seven weeks, when insidious symptoms of weakness, pallor, and tarry stools again appeared. She was readmitted on March 3, 1953, with marked pallor and slight generalized edema. The blood count showed 6.8 gm. (40%) of hemoglobin per 100 cc., and 2,640,000 red cells. She was given a total of 3,000 cc. of blood during the next 10 days. Clinical improvement was satisfactory, and on March 16 the blood count showed 15.4 gm. (90%) of hemoglobin per 100 cc., and 5,200,000 erythrocytes.

Operation was performed March 17. The stomach was entirely normal except for the presence of a short-loop, isoperistaltic, retrocolic gastrojejunostomy. The duodenum was dilated to a diameter of 6 cm. from its beginning just distal to the pylorus all the way to its terminal portion, where it ended blindly in a complete atresia under the superior mesenteric vessels. There was a mere fibrous string from this point to the ligament of Treitz. At this point, normal jejunum appeared and extended 6 cm. to the gastrojejunostomy stoma. The 4 cm. stoma was well placed beneath the transverse mesocolon and was mechanically correct. No definite ulcer could be felt, but there was some thickening on the posterior wall of the stoma. Thorough examination of the colon and of the small bowel distal to the anastomosis revealed no lesion. The gastrojejunostomy stoma was opened along its anterior margin disclosing a 7 mm. ulcer on the posterior wall exactly at the line of union of gastric and jejunal mucosa. The ulcer was 4 mm. deep and surrounded by moderate induration. The entire circumference of the stoma, including the ulcer, was excised. The gastric and jejunal stomata were closed, as was also the opening in the transverse mesocolon. The jejunum, at a point 15 cm. distal to the ligament of Treitz, was then joined to the anterior wall of the duodenum 8 cm. distal to the pylorus, with use of a side-to-side anastomosis to create a 3 cm. stoma. The pathologist reported a 7 by 4 mm. benign ulcer exactly at the point of surgical union of stomach and jejunum, the base of the ulcer extending into the muscular layer.

The patient withstood the operation well and left the hospital on the fifth postoperative day, taking a full bland diet and tolerating it well. At the time of discharge the blood count showed 15.2 gm. (91%) of hemoglobin per 100 cc., and 5,570,000 erythrocytes. She has remained entirely well and free of symptoms on a totally unrestricted regimen.

COMMENT

It is interesting that this child was completely well and normal for 11 years 3 months following a gastrojejunostomy. This operation was performed when she was 4 days old for complete duodenal atresia considerably distal to the ampulla of Vater, an obstruction which necessarily shunted all biliary, pancreatic, and duodenal

secretions back through the pylorus into the stomach. The sudden dramatic appearance of massive gastrointestinal hemorrhage was the first symptom of trouble. Actually, recurrent bleeding and the resulting anemia and weakness were her only symptoms. At no time did she have pain or indigestion. It seems incredible that she could three times suddenly exsanguinate 60 to 70% of her circulating blood from a lesion which was half in the stomach without once having hematemesis or vomiting of any kind. Three series of gastrointestinal x-rays failed to demonstrate a marginal, gastric, or duodenal ulcer. This encouraged the hopeful expectation of possibly finding a Meckel diverticulum as the easily correctable source of her bleeding. My colleagues and I were also hopefully remembering the frequency of multiple congenital anomalies. However, the preoperative provisional diagnosis was gastrojejunal ulcer.

SUMMARY

A case of gastrojejunal ulcer is reported in a child who previously had a gastrojejunostomy for duodenal atresia.

Three massive painless gastrointestinal hemorrhages with melena but no vomiting were the only symptoms.

Gastrojejunal ulcer is a possible complication of gastrojejunostomy in children as well as in adults.

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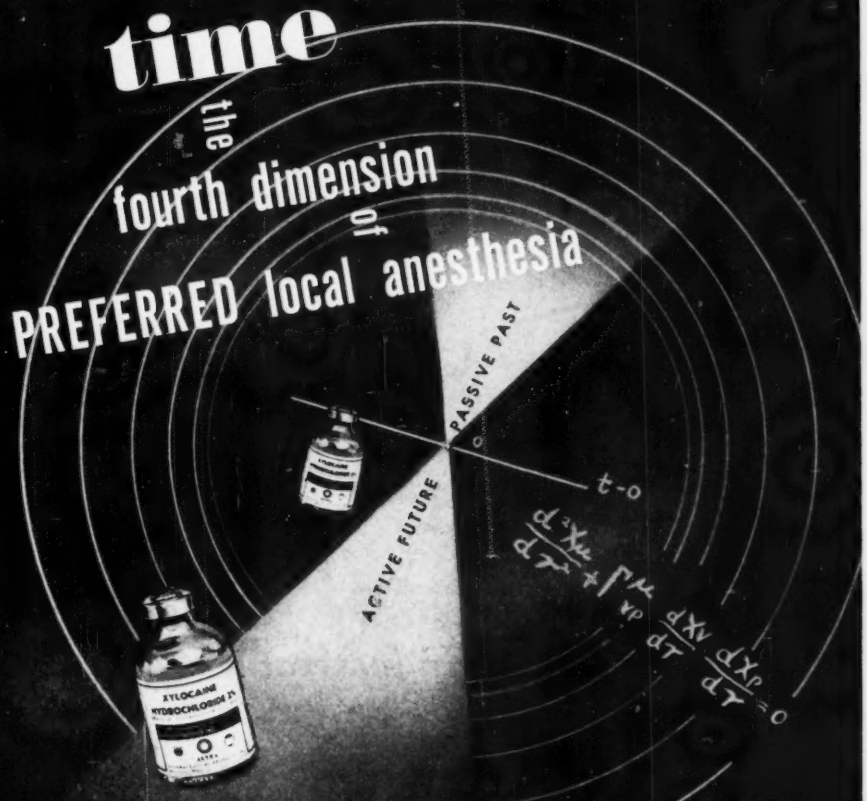

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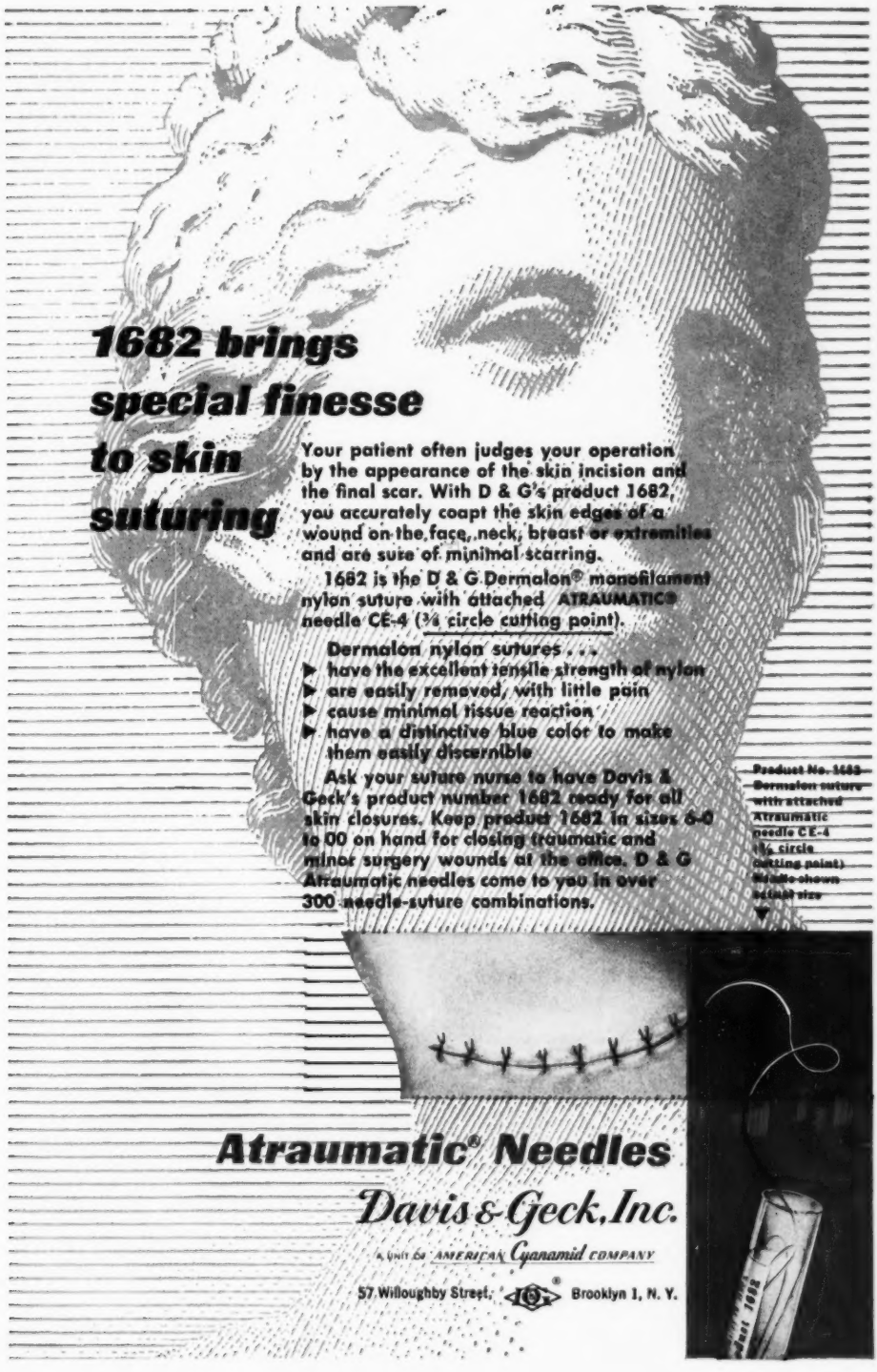

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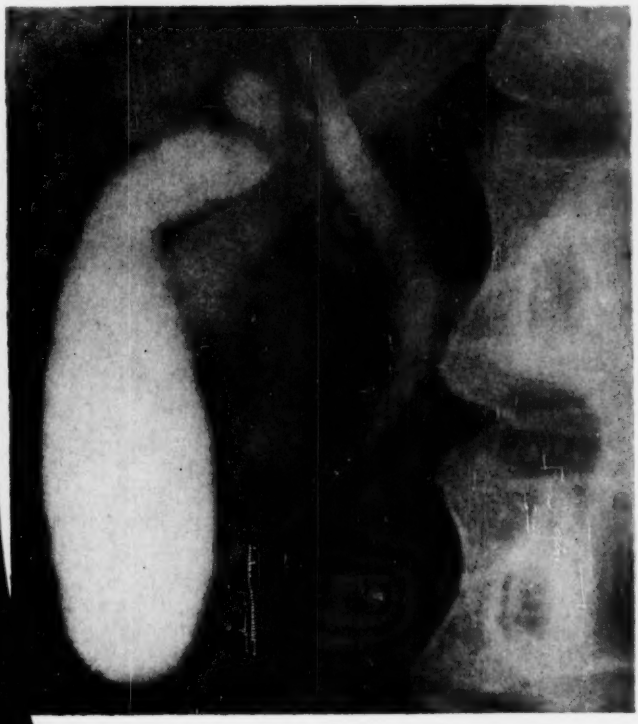

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